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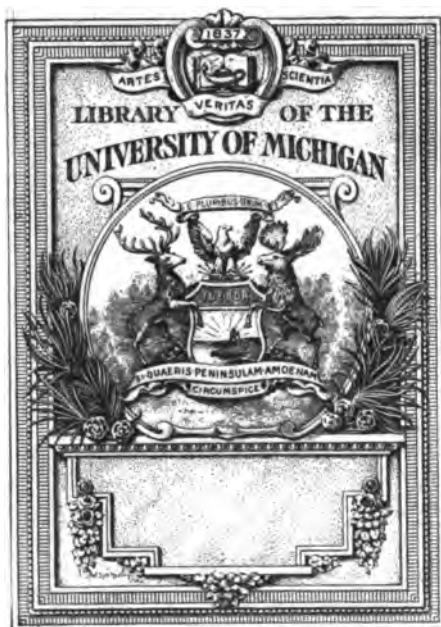
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PLATE I.

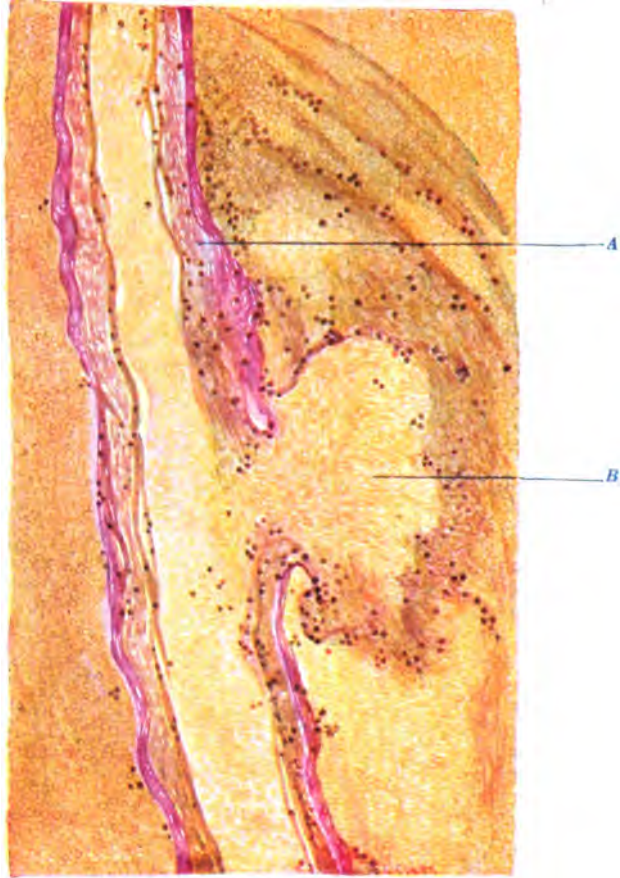


FIG. 6.—CASE XIII.—Vessel and false aneurysm in longitudinal section. *A.* Vessel wall with advanced degeneration of the intima and media on the side bearing the aneurysm. *B.* False aneurysm, largely filled by blood. (B. and L. Oc. I, Obj. $\frac{2}{3}$.)

[See p. 282]

UoR N

INTERNATIONAL CLINICS

A QUARTERLY

OF

ILLUSTRATED CLINICAL LECTURES AND
ESPECIALLY PREPARED ORIGINAL ARTICLES

ON

TREATMENT, MEDICINE, SURGERY, NEUROLOGY, PÆDIAT-
RICS, OBSTETRICS, GYNÆCOLOGY, ORTHOPÆDICS,
PATHOLOGY, DERMATOLOGY, OPHTHALMOLOGY,
OTOLOGY, RHINOLOGY, LARYNGOLOGY,
HYGIENE, AND OTHER TOPICS OF INTEREST
TO STUDENTS AND PRACTITIONERS

BY LEADING MEMBERS OF THE MEDICAL PROFESSION
THROUGHOUT THE WORLD

EDITED BY

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Treatment

IMMUNIZATION AGAINST TYPHOID FEVER

WITH A STUDY OF PREVENTIVE INOCULATIONS

BY HARLAN SHOEMAKER, M.D.

PHILADELPHIA

Historical.—This very interesting subject has been developed mainly through the efforts of Sir A. E. Wright in his endeavor to protect the British Army from the ravages of typhoid fever during the Boer War. Wright gratuitously prepared 400,000 vaccines, and personally gave 4000 inoculations. He states in his "Short Treatise on Antityphoid Inoculations," published in London, 1904, by Archibald Constable & Co., Ltd., that the subject had been destined, so far as he was concerned, to remain indefinitely inoperative. However, upon a visit made to Prof. R. Pfeiffer's laboratory in Königsberg, where Wright observed, for the first time, substances in the blood of two men who had been previously inoculated with typhoid bacilli, killed by heat, he saw immediately the possibility of prophylactic inoculation. Subsequently, Wright inoculated two men in a manner similar to the inoculations made by Pfeiffer, and published his results in the *Lancet*, September 19, 1896.

Haffkine had previously used attenuated living cultures of the cholera vibrio to produce immunity against this disease, which fact is well known to all. Wright considered this method of immunization to be attended with too great a risk when applied toward immunity against typhoid. Recently this method of Haffkine's has been advocated by Strong of Manila and Kolle of Germany, for the preparation of bacterial vaccines such as typhoid, plague, and cholera. Both Wright and Pfeiffer have considered the foregoing procedure to be attended with too much risk to be used as a routine.

Great opposition developed in the British Army to the Wright method of inoculation with dead cultures of the *Bacillus typhosus* as protection for the British soldiery against typhoid, and consequently a commission was appointed to investigate thoroughly and improve upon Wright's method.

Statistics.—Great difficulty was experienced, subsequent to the Boer War, in gathering and appraising the statistics of inoculations against typhoid, as these so-called vaccinations were often confused with the Jennerian vaccination against smallpox. Furthermore, during the rush and confusion of army life at the front, every continued fever was reported as typhoid.

The German South African campaign has provided the best statistics as to the immunity conferred upon large numbers of troops in an endemic typhoid area. The men were inoculated after the manner of Pfeiffer and Kolle. Some received three inoculations of a typhoid bacterial suspension killed by heat at 63° C. Some received but one; others, two inoculations. For the most part they were all inoculated at least twice before boarding the transports. All inoculations were voluntarily obtained by lectures and demonstrations before the recruits, given by the medical officer.

There seems to exist much fear in the minds of the German medical officers over the lowered resistance toward typhoid which is supposed to exist in the inoculated subject shortly after the inoculation. This condition was called by Wright the negative phase.

Kuhn ¹ reports the statistics of inoculation in the South African campaign of the German Army. I take it for granted that everyone is so familiar with the very rapid spread and malignancy of typhoid fever in armies while in the field, more especially those corps recently recruited, that it is unnecessary to repeat any such statistics in this paper. A. Netter ² has reviewed this subject thoroughly.

Kuhn also goes into this subject completely. During this campaign 7287 men were inoculated, and 9209 were not. The first inoculation was 0.5 c.c. of vaccine; the second was 1 c.c.; and the third was 1.5 c.c. All were given subcutaneously. He found that

¹ Die Deutsche Militärärztliche Zeitschrift, April 24, 1907.

² Bull. de l'Institute Pasteur, 1906, vol. iv, p. 873.

17 per cent. had vomited after the first inoculation, 2 per cent. had high fever (104° F.) and malaise for forty-eight hours. The second inoculation did not produce symptoms as severe as the first, while the third injection was unattended with any reaction whatsoever.

The presence of so great a body of typhoid-immune men, together with the number of acquired immunities in those recovering from the disease, reduced the number of enteric cases from 226 in 1904 to 43 in 1907.

Card records of 1277 cases of typhoid with precise data were available for analysis in February, 1907. Of this number 906 represent cases of enteric fever amongst men who were not inoculated, and 371 cases amongst the inoculated. Therefore the cases amongst the uninoculated are equivalent to 9.84 per cent. of the strength of the uninoculated, and amongst the cases of the inoculated, to 5.09 per cent. of the inoculated strength. Differentiated according to severity of attack, Dr. Kuhn presents the following statistics:

	Uninoculated.		Inoculated.	
Light cases	331	(36.55 per cent.)	186	(50.13 per cent.)
Moderately severe.	225	(24.85 per cent.)	96	(25.88 per cent.)
Severe	234	(25.80 per cent.)	65	(17.52 per cent.)
Fatal	116	(12.80 per cent.)	24	(6.47 per cent.)
<hr/>				
Total	906	(100.00 per cent.)	371	(100.00 per cent.)

These figures show a higher percentage of light attacks and a lower percentage of fatal attacks amongst the inoculated than amongst those not inoculated. The following shows the period elapsed after inoculation, at which the inoculated contracted the disease:

Light Cases.

	Once inoculated.	Twice inoculated.	Thrice inoculated.
One week	1	2	0
Two weeks	1	2	0
Three weeks	0	1	0
Four weeks	1	2	0
Two to six months	30	52	23
Seven to twelve months	13	20	12
Over twelve months	13	12	1
<hr/>			
Total	59	91	36

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Moderately Severe Cases.

	Once inoculated.	Twice inoculated.	Thrice inoculated.
One week	0.	0	0
Two weeks	0	0	0
Three weeks	0	0	0
Four weeks	0	0	0
Two to six months	11	22	11
Seven to twelve months	7	11	7
Over twelve months	5	14	8
—	—	—	—
Total	23	47	26

Severe Cases.

	Once inoculated.	Twice inoculated.	Thrice inoculated.
One week	2	2	0
Two weeks	0	0	0
Three weeks	0	0	0
Four weeks	0	0	0
Two to six months	12	12	4
Seven to twelve months	2	10	3
Over twelve months	11	4	3
—	—	—	—
Total	27	28	10

Fatal Cases.

	Once inoculated.	Twice inoculated.	Thrice inoculated.
One to four weeks	0	0	0
Two to six months	5	3	1
Seven to twelve months	5	1	1
Over twelve months	4	4	0
—	—	—	—
Total	14	8	2

Number of cases amongst inoculated and percentage respectively, of those inoculated once, twice, and three times.

	Once inoculated.	Twice inoculated.	Thrice inoculated.
Grand Total...123 (6.31 per cent.)	174 (4.81 per cent.)	74 (4.69 per cent.)	

Dr. Kuhn regards these results of sufficient importance to warrant the conclusion that those inoculated once suffer more than those inoculated twice; and those inoculated twice, more than those inoculated three times. When the above percentages are compared with that of the uninoculated, viz., 9.84 per cent., a good idea of the results of inoculation may be obtained.

The following table shows clearly the favorable effects of the greater number of inoculations:

Percentage of Cases.

	Once inoculated.	Twice inoculated.	Thrice inoculated
Light cases	31.72	48.93	19.35
Moderately severe cases	23.95	48.96	27.09
Severe cases	41.54	43.09	15.40
Fatal cases	58.33	33.33	8.33

As none of the cases amongst those inoculated three times occurred within the first four weeks Dr. Kuhn thinks it is questionable whether a negative phase exists after a third inoculation, but whether it is the third inoculation itself or the greater period which has elapsed since the first and second inoculations he is not prepared to state.

Duration of Immunity.

Number and percentage of cases occurring within months after inoculation as noted.

	Light.	Moderately severe.	Severe.	Fatal.
Two to six....105	(56.45)	44 (23.65)	28 (15.05)	9 (4.85)
Seven to twelve..45	(48.91)	25 (27.17)	15 (16.31)	7 (7.61)
More than twelve 26	(32.91)	27 (34.88)	18 (22.78)	8 (10.13)

Dr. Kuhn concludes that immunity is lost one year after inoculation, his reason being the increase in the moderately severe, severe, and fatal cases combined with a decrease in the light cases. The severer cases amongst the inoculated after one year show almost as high a proportion as those not inoculated.

Dr. Kuhn further points out that complications are twice as frequent amongst the uninoculated as the inoculated; that a considerably smaller number of the inoculated contract enteric fever as compared with the uninoculated; that the course of the disease amongst the inoculated is on the average much more favorable than amongst the uninoculated.

Investigation of British Commissions.—The appointment of a commission by the British war office to investigate thoroughly the claims made by Wright for his method of immunizing the army was a step forward in arriving at a reliable means of producing an immunity against typhoid fever. So far the findings of this commission³ are confirmatory of Wright's experience, and still

³ Journal of Hygiene, 1905.

retain essentially his technic, with minor modification. In the report a careful estimate is made of the effects produced in the blood stream by dosage upon, (1) a negative and positive phase; (2) stimulins *vs.* opsonins; (3) bactericidal substances; (4) bacteriolytic substances; and (5) agglutinins.

The commission also made arrangement to send a qualified observer from the laboratory with the troops *en route* for India, so that the observations begun might be correctly reported.

Lt. Luxmoore⁴ reported his observations on the 17th Lancers as follows: Shortly after arrival in India, 63 cases of typhoid occurred in the regiment; only two of these were among the inoculated, and they had received but one dose. These statistics are meager when compared with Dr. Kuhn's tables, but the relative merits of inoculation in the British and German armies is clearly brought out. The English statistics to-day do not show a single death amongst the inoculated.

Negative and Positive Phases.—The third report of the British commission,⁵ as well as the general consensus of opinion given at the International Congress of Hygiene, Berlin, September, 1907, held that the negative phase of Wright was of doubtful existence.

Stimulins vs. Opsonins.—The members of the British commission, in their second report, found an increase in the phagocytic activity produced by a heated (60° C.) blood-serum over that produced by the unheated serum. The commission has designated the activating substance in the heated blood-serum as stimulin.

Klein⁶ called attention to this phenomenon, and first suggested the cause. He thought it probable that the members of this commission were working with an old strain of the *Bacillus typhosus* which had become modified by long artificial propagation.

Dean, of the Lister Institute, also reversed the findings of the commission in this particular. He used a strain of the *Bacillus typhosus* recently obtained from the blood of an infected patient. While working with virulent and non-virulent strains of *Bacillus typhosus* he confirmed the original Wright theory that opsonin—unheated blood-serum—created a greater phagocytosis than blood-

⁴ Journal Royal Army Medical Corps, 1907, vol. viii, p. 492.

⁵ Jour. Royal Army Med. Corps, 1908, vol. xi.

⁶ Johns Hopkins Bulletin, 1907, vol. xviii, p. 245.

serum heated to 60° C. These findings have been accepted by the British commission and the reverse was found to be true when Dr. Dean used the old strain sent him by the members of the commission.⁷ An investigation was immediately started to determine the nature and effects produced by various strains of *Bacillus typhosus*, viz., virulent strains, and non-virulent strains which had been recently recovered from the blood of patients suffering from typhoid fever. Other than the result already mentioned, nothing has been added to our knowledge of an additional immunity to be secured by the use of the above-mentioned strains, although various Indian writers, as well as Pfeiffer of Germany, have expressed their views in favor of a vaccine made from a strain of *Bacillus typhosus* indigenous to the region in which the exposure to the disease is most likely to occur.

Preparation of Vaccine.—The vaccine used for the first inoculation was prepared by washing off, with an 0.85 per cent. saline solution, the twenty-four hour growth from three agar slants, and treating the same in a water-bath at 53° C. for one hour. This degree of heat had been found necessary by the British investigators to kill the *Bacillus typhosus*. Here I found my chief difficulty, because the vaccine was not killed by exposure to this degree of heat. It was finally killed by exposure to 55° C. for one hour. I account for this variation in the thermal death point of the organism in question by its extreme motility and its recent cultivation from the blood-serum.

The vaccine for the first inoculation was prepared from the sixtieth generation. As no stock was prepared from this brew, the second vaccine was prepared from about the eightieth generation. Greater difficulty was experienced in killing the second vaccine than the first one; 56° C. would have been sufficient to perfect this brew, but the water-bath finally reached 59° C. before the end of one hour. Wright originally heated his vaccine to 60° C.

Preservation of Vaccines.—Harrison⁸ gives the results of very elaborate experimentation in the preservation of vaccines from various bacterial suspensions. These vaccines were desiccated over sulphuric acid, and the pulp used dry or extracted by means of

⁷ Journal Royal Army Med. Corps, vol. xi, 1908.

⁸ Jour. Royal Army Med. Corps, 1907, vol. viii, p. 472.

distilled water and filtered. Chloroform, alcohol, and glycerin were also used as preservatives.

Lysol, which is a saponified tricresol, gave the best results, chiefly on account of the small quantity necessary for preservation, as well as its non-toxicity. These experiments satisfactorily proved that lysol in 0.20 per cent. would sterilize living organisms when added to the vaccine as test objects. *Bacillus subtilis*, *anthracis*, and *tetani* were sterilized in the solution in five days. Upon the addition of saliva to the solution containing 0.20 per cent. lysol, no living germs were found on the seventh day. With ordinary care in handling, 0.25 per cent. lysol is considered a very safe margin, and all that is necessary to free a vaccine from any accidental contamination from the air.

Age of Vaccines.—The duration of active immunizing substances in vaccines which have long been preserved has been given some attention in the third report of the British commission. A vaccine returned to them from the tropics was found to have lost nearly all its activity. This led to observations on vaccines kept at 0° C., 22° C., or room temperature, and 37.5° C., or blood heat. All of the vaccines so treated lost, largely, their activity after three months, although that kept at room temperature was least affected. One would naturally suppose that a vaccine killed at 53° C. for one hour would resist any natural temperature for a period longer than three months. Autolysis, or further saponification by the lysol, may be the cause of this loss of activity in a bacterial vaccine.

The effects of exposure to various degrees of heat on the immunizing substance in the bacterial body are suggested by the following observations made while producing immunity with various bacterial vaccines: Inoculations with a vaccine prepared by heating to 90° C. produced no effects—neither clinical, subjective, nor laboratory phenomena. Gradual reductions in the temperature to which the vaccine was exposed produced, upon inoculation, increasing local and general constitutional symptoms, and a higher opsonic index.

Thermal Death Point.—A safe rule to follow in the preparation of a bacterial vaccine which retains the greatest immunizing power is to ascertain the least degree of heat necessary to kill the strain of the bacterium used.

A number of products, other than the whole bacillary substance, have been used as means toward producing an immunity against a specified organism, chief of which are the serums derived from the blood of horses inoculated over a period of time with cultures of varying toxicity and viability. Chantemesse of Paris, at the International Congress of Hygiene, Berlin, September, 1907, reports a mortality of 4.3 per cent. amongst 1000 cases of enteric fever treated with serum from a horse which required three years to be immunized. At the same time in the other Paris hospitals, the mortality amongst 5000 cases of enteric fever reached 17 per cent.

These are very startling figures and indicate results which, when compared with the work of Richardson,⁹ are even more amazing. Richardson's observations over eight years of experience in treating enteric fever with serums and bacterial products confirm a rather high mortality rate.

Vaughn of Ann Arbor has split the bacterial body into toxic and non-toxic proteids. For the latter he claims specific immunizing powers. One physical factor, to my mind, is operative against these substances. The bacteria are extracted in a Soxhlet tube by means of boiling alcohol at 70° C. As this degree of heat nearly robs the bacillary body of all of its antigenetic properties, I cannot conceive of any specific immunizing power remaining in the cleavage products of the germ.

Foreign authors have offered similar products variously derived, some without the aid of heat, as a means toward producing immunity, only to be met by strong opposition from Pfeiffer. He sees the need of an immunity against all the bacterial proteids, in order to give adequate protection from the disease.

Method of Administering Vaccine.—Vaccine has been given subcutaneously, and generally on the arm. This method of administration has become the one of choice. More recently numerous experiments have been made to produce immunity by taking the vaccine by mouth. Reactions similar to those produced in subcutaneous inoculations have been observed for a short time in the blood-serum. However, the gastro-intestinal symptoms have been so severe that the method has been invariably abandoned. The idea of taking vaccine by the mouth would grow out of the ease with

⁹ Mass. Med. Society, 1907.

which it could be administered and the avoidance of much unpleasant local reaction.

I think it a fairly safe conclusion that all active vaccinations must be attended with more or less local reaction in order to produce those substances in the blood which confer the immunity desired.

As I shall endeavor to point out, in the curve of agglutinins observed in the inoculation of four subjects, the persistence of some local induration at the site of inoculation is responsible in maintaining, possibly in developing, for some time, protective substances in the blood. It is well known that the agglutinins and bacteriotropic substances rapidly diminish after the third week of typhoid fever. After convalescence has once become well established, there is a rapid disappearance of all protective substances.

Two methods recently put forth may add something more to our knowledge as other workers have more experience with them. One is a method of determining the phagocytic activity of the blood-serum as devised by Klein of Johns Hopkins, from whom I have previously quoted. The other is the method known as deviation of the complement. This method of estimating immunity has been modified by Wasserman and Kolle.

A last word comes from the Royal Army Medical Corps Commission in its third report, relative to an increased phagocytic power of the blood-serum of one ill with typhoid as a favorable prognostic sign.

CLINICAL OBSERVATIONS

On November 9, 1908, I inoculated four persons—two nurses, a doctor, and myself—with a typhoid vaccine. The vaccine was estimated, after the manner of Wright, to be 400,000,000 germs to the cubic centimetre. The germ being extremely motile was enumerated with some difficulty. The addition of formalin had a tendency to produce slight clumping. One c.c. of a bouillon culture was not fatal to a 250 Gm. guinea-pig when injected into the peritoneum.

CASE I.—M. B., nurse. First inoculation, 0.33 c.c., was given subcutaneously at the insertion of the deltoid tendon in the humerus. In four hours a local reaction began with pain, swelling, heat, and

redness. During the second 24 hours the temperature rose to 101° F., accompanied by malaise and general aches. She vomited. She was off duty two hours. During the third 24 hours there were sweats. The temperature became normal, and the local reaction began to disappear.

CASE II.—N., nurse. Dose and symptoms, both local and general, the same as in Case I.

CASE III.—Dr. M. Weight 200 pounds. Dose 0.66 c.c. Local reaction about site of inoculation very angry. Constitutional symptoms were marked. Temperature rose to 102° F. He vomited, and went to bed. The symptoms passed off in about the same order as those in Cases I and II.

CASE IV.—Dr. H. S. Weight 180 pounds. Dose 0.66 c.c. Local reaction extended from the shoulder to the elbow, red and swollen, but not angry. Constitutional reaction was slight. Temperature was 101° F. There was no prostration. He did the usual amount of work. He had a profuse sweat two nights succeeding vaccination, with a disappearance of the general symptoms. An indurated area about the size of a silver dollar remained at the site of inoculation about fifteen days.

The profound reaction in Case III could be accounted for by a rather violent game of tennis which the doctor indulged in immediately following inoculation. He used the inoculated arm in play.

The Second Inoculation.—The proper interval for a second inoculation, especially if we accept the negative phase of Wright, is when the agglutination curve is ascending. The agglutinins begin to show in the blood on the ninth day, and reach a maximum on the eleventh day. I was unable to fulfil these conditions, as I attempted to make a fresh vaccine for the second inoculation, and I had some difficulty in killing the vaccine, which delayed this inoculation until the agglutinin curve was falling.

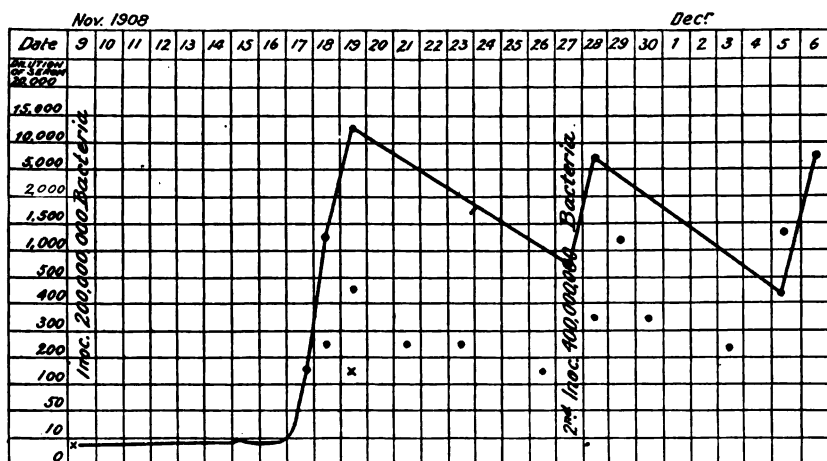
Twice the quantity given in the first dose was used. No constitutional reaction was noted in any of the subjects inoculated. A well-defined local reaction appeared shortly after injection, and disappeared about the third day. An area of induration at the site of injection, much smaller than that attending the first inoculation, remained a number of days.

Protective Substances in the Blood Serum.—Prior to the first

inoculation the highest dilution of the blood-serum with which it was possible to produce agglutination varied from 1:7 to 1:10 in the four subjects. On the eleventh day after the first inoculation, the highest agglutination obtained was 1:12,872. This high-tide mark fell somewhat, but not as low as the curves obtained by the English Commission.

The second inoculation produced a rising curve, 1:8,000 apparently being its limit, which I think due entirely to stimulation. About the tenth day after the second inoculation another

Fig. 1.



Development of agglutinins following inoculations of a vaccine prepared from a non-virulent strain of *B. typhoeus*. X, eleventh day, an ideally proper time for second inoculation.

rise is noted in the agglutination curve. This produces a sort of staircase arrangement (see chart).

The curve described in the chart is that produced by the exhaustion of the agglutination reaction. The other dots show several estimations of the agglutinin in which the end reaction was not determined. The continued high wave of the agglutinin curve is in contrast to those of Wright, where the descent is more abrupt, and may be accounted for by the persistence of an indurated area at the site of inoculation.

While immunizing a patient against *Staphylococcus pyogenes aureus*, thinking that I had produced an abscess, I had an occasion to incise an indurated area produced by vaccine. I found a cellu-

litis from which exuded a sterile serum. This serum was nearly devoid of opsonin, whereas the patient's blood was unusually high in opsonin. In the continuous production of agglutinins within this indurated area may be found the cause of the maintenance of the agglutination curve.

Bactericidal Power.—In my observations I found that the blood-serum exhibited, after inoculation, a bactericidal power in a dilution of 1:20. Viable bacteria when mixed with immune blood-serum in the above dilution failed to produce colonies when spread over an agar plate, and kept at 37.5° C. for twenty-four hours.

Bacteriolysis.—The immune blood-serum of my cases diluted 1:4 to 1:6 and mixed with living *Bacillus typhosus* either produced spherulated forms or a complete disappearance of the organisms. This was determined in microscopical examination by lateral illumination of the fresh serum, and by spreading the serum mixture upon cover slips and staining with methylene blue.

Subsidence of the Phenomena.—The agglutination reaction has subsided within normal limits six months after inoculation, but in its place has come an increase of one-tenth of the body weight in those inoculated. This growth was somewhat simultaneous in the four individuals inoculated.

CONCLUSIONS

1. Unquestionable evidence exists regarding the immunity conferred by inoculation.
2. Two or more inoculations are necessary to make the immunity of some duration.
3. More investigation of the blood in typhoids for the strength and duration of protective substances is necessary.
4. At present the method for determining the strength of a vaccine is liable to considerable error.

MINERAL WATERS IN THE TREATMENT OF SYPHILIS

BY CARRON DE LA CARRIÈRE, M.D.

HYDRARGYRUM is the sole remedy for syphilis; the difficult point is to succeed in saturating the system with it for several years, with a minimum of harm to the patient and a maximum of effect on the virus.

No thermal cure has any antisyphilitic action, properly so called—the hopes that had been placed in the waters of Aulus and St. Nectaire were not well founded—but any cure, whether of chloride, arsenical, or sulphurous waters, capable of improving the condition of the system, of counteracting the anæmia and constant demineralization of a syphilitic patient, can be considered a useful auxiliary to the treatment by mercury.

Sulphurous waters deserve the first place, for in addition to their general and powerful action on the patient's nutrition, they have a special action on the only specific remedy, mercury: they increase the tolerance of the system toward this agent, enable it to be used in enormous doses without risk of intoxication, and thus strengthen very considerably its effect in the fight against the treponema.

In order to understand the way in which sulphurous waters act, it may be useful to recall the transformations that mercury undergoes in the body.

The hypothesis of Mialhe warrants our believing that: (a) On coming into contact with the chloride of sodium of the liquids of the body the different mercurial compounds are transformed into a double chloride of sodium and mercury; (b) this bichloride combines with the albuminoid substances of the tissues to form albuminates of mercury; (c) these chloro-albuminates, or oxychloro-albuminates of mercury are soluble but very unstable. A portion circulates in the blood and is rapidly eliminated in the urine; another is transformed into an insoluble compound, remains fixed

in certain organs (liver, kidneys, spleen, and lymph-nodes), and is eliminated very slowly several weeks or months after the administration of the remedy.

What is the action of sulphur waters on these albuminates of mercury? The sulphur combines with the insoluble albuminate of mercury and forms a soluble sulphate of mercury. The consequences of this transformation are considerable from a therapeutic point of view: the insoluble mercurial albuminate remaining fixed in the tissues is probably inert or has only a very slight efficacy; but when it is rendered soluble again it is capable of being absorbed once more, passes into the circulation, and its elimination is facilitated by the fact that a sulphur cure stimulates the functions of liver and kidneys.

In this way a steady current of mercury is induced, whose effect on syphilitic lesions is very great, any excess of mercury being neutralized by the sulphuretted hydrogen as it is produced, and then eliminated; it is therefore possible to understand how such enormous doses as 20 grammes of mercurial ointment and 5 to 6 centigrammes of benzoate or biniodide of mercury per diem in injections may be tolerated by patients, and how tenacious and relapsing lesions may yield to the action of this intensive and uninterrupted treatment.

This dissolution of the albuminates of mercury by the action of sulphur explains the following experiment due to Astrié. When corrosive sublimate is added to blood-serum an insoluble white precipitate is thrown down. This precipitate, however, dissolves by the addition of some form of sulphur—sodium sulphide, hyposulphite or sulphate of soda—the less oxidized the sulphurous product the quicker and more complete the reaction. The action of sulphuretted hydrogen is almost instantaneous, next in order come sodium monosulphide, hyposulphite and sulphite.

In practice this action of sulphur waters on the syphilitic patient has a threefold effect that can be summed up in the following propositions.

1. The sulphur waters act on the accumulation of inert mercury in the organs and render it soluble. This mercury then regains its power over the body for a long period after its administration.

Thus, patients who had had no mercurial treatment for a

month and a half, fourteen months, and eighteen months, and whose urine no longer contained a trace of mercury, and who were put on a sulphur cure either at their home or at a natural mineral water Spa, were found after a few days of sulphur treatment to show signs of mercury again in the urine and a slight degree of stomatitis.

In a case where there were deep serpiginous ulcerations, nine injections of calomel produced no improvement, and there was stomatitis. The mercurial treatment was then stopped, and nothing but Uriage water given, with the result that the urine showed an abundant evacuation of mercury with rapid improvement in symptoms, and the ulcerations healed up in a month without further mercurial treatment.

It therefore seems as if the mercury had been stored up and was inactive, so to speak, in the organs, but had been set in motion and eliminated by the sulphur water.

2. The sulphur waters prevent or cure signs of mercurial intoxication, and especially salivation, by the rapid elimination of mercury which they induce. Thus if a syphilitic patient with mercurial stomatitis takes a sulphur treatment, such as two glasses of Uriage water, for instance, stomatitis disappears rapidly; even if the mercury is continued.

The explanation of this fact is not difficult. Mercurial intoxication is due to the accumulation in the system of a too great amount of mercury; the sulphur waters, by dissolving the mercury, give rise to rapid elimination and prevent its being stored up in the organs. If the mercury does not accumulate it cannot cause trouble even in large doses.

3. A syphilitic patient treated by sulphur waters will stand an amount of mercury two or three times greater than the usual doses without signs of intoxication, even though he may be very susceptible to this remedy.

Thus, a patient who had not been able to stand an efficacious dose of mercury, and who even in slight doses presented signs of intolerance, such as stomatitis and diarrhoea, became tolerant to the remedy as soon as the sulphur cure was combined with the specific treatment.

Another patient had no trouble in taking the ordinary average

dose, but the result obtained was not satisfactory; as soon, however, as he was put on sulphur water, improvement was rapid.

A third man, with serious lesions, required an intensive treatment, but stomatitis made large doses impossible; he was then put on sulphur water and became tolerant to mercury with a rapidity and to a degree that were surprising.

It is in this manner that at the sulphur Spas the physicians succeed in giving to their patients enormous quantities of mercury daily without any trouble. This exceptional tolerance is explained by the steady and rapid elimination of the mercury. The patient is, so to speak, kept saturated with mercury, a condition that might be dangerous if the sulphur did not act as an evacuator and prevent accidents. Besides this, even when mercury is only given in ordinary doses, since the whole amount is utilized, and not partially stored up, we are able with equal amounts to obtain by means of a sulphur cure effects that are more rapid and complete.

Which syphilitic patients are we to send to sulphur Spas?

1. The test treatment has been definitely abandoned as useless and dangerous. It was based on a property attributed to sulphur water of giving rise, in a syphilitic patient who was not cured, to an explosion of specific accidents. Thus a syphilitic patient wishing to marry was sent to a sulphur Spa; if nothing appeared during the treatment it was thought that he might consider himself as definitely cured. This test has no value whatever and has caused many a disaster. The number of patients who have remained without symptoms during and after a sulphur cure, but who have later on had the most serious specific manifestations, is legion.

2. A sulphur cure increases tolerance for mercury and counteracts the anæmia and malnutrition of the syphilitic organism; it is therefore a most useful complement to the usual treatment of syphilis at any period. The sulphur cure can be advised even at the beginning of the disease, and every syphilitic patient would gain by such a course, now and then, even when he is apparently perfectly well.

3. But in certain cases this cure is more especially advisable: (a) Whenever mercury is badly tolerated in ordinary doses, or when in spite of tolerance the result obtained is insufficient; (b) whenever an intensive mercurial treatment is indicated, *e.g.*, early

malignant syphilis, gummata appearing soon after the chancre, localizations in the nervous system, tabes, incipient general paralysis, and in syphilis with tenacious lesions that do not yield to treatment, such as palmar psoriasis, lingual sclerosis, recurrent mucous patches, etc.

The choice of a Spa in France lies among the strong sulphurous waters of the Pyrenees and the Alps: Aix, Amélie, Barèges, Cauterets, Challes, Luchon, Uriage, and Vernet. Professor Garrigon thinks that the waters richest in hyposulphite, such as Aix or Olette, are the best; but experience really shows that as regards efficacy all of these Spas are about equal, whatever may be the specific localization, even if it affects the nervous system. Distinctions between them is really a mere question of shades, depending either on the way in which the water is administered, or on the patient's constitution. In general terms it can be stated: (a) that waters that are readily tolerated by the stomach (Uriage or Challes) are specially active; (b) that lymphatic and scrofulous patients do best at Challes, Uriage, and Barèges; (c) that arthritic and neuropathic patients do best at Aix, Cauterets, or Luchon.

Challes, with its cold water at 13° C., containing the most sulphur, iodine, and bromine of all this class of waters, presents the advantage that it is readily tolerated by the stomach, even in children, thanks probably to the sodium bicarbonate that it contains.

Uriage, an isotonic, aërated, sodium chloride sulphur water, is likewise well tolerated by the digestion. These two Spas, Uriage and Challes, should be given the preference in treating hereditary syphilitic children. Luchon deserves notice on account of its specialty of inhalations, which enable the waters to be given easily and even pleasantly by means of the warm sulphurous vapors, which are always well tolerated, and whereby the sulphur is absorbed in a liquid state; furthermore, the general comfort at this Spa, as well as its situation in the centre of the finest excursions in the Pyrenees, makes it one of the most desirable places to which patients can be sent.

Barèges, with its high elevation of 1232 metres, and its powerful polysulphurous water, is indicated in malignant syphilis with ulcerous, tenacious lesions of the bones in profoundly debilitated adults.

Cauterets has, like Barèges, a high altitude, 923 metres, and also a wide variety of sulphur waters and a sufficient amount of modern comfort; it is, furthermore, situated in an admirable region, the centre of a multitude of walks and excursions.

Aix exceeds all the other Spas in its abundance of water, its differences in mineralization, and the great variety of ways in which the waters are put to use.

Amélie and Vernet, on account of their southern position and warm climate, furnish useful resorts for patients who require a sulphur cure during spring, autumn, or even winter.

In order to profit by the increased tolerance for mercury under the influence of the sulphur cure, the majority of authors advise that the two treatments, thermal and hydrargyric, should be carried out simultaneously. Dresch, of Aix, has, in a number of interesting publications, recommended the intercalary thermal cure, that is to say, one with no mercurial treatment during the interval between two specific cures. He thinks that the thermal treatment should vary according to the state of the syphilis. During the first period, during which the patient is each year put through the mercurial treatment, the thermal cure should, in the great majority of cases, be intercalary. Later on, when mercurial treatments become much less frequent, on account of the latent state of the diathesis, it will be found a wise precaution to combine the thermal cure with the specific treatment.

DIAGNOSIS AND TREATMENT OF PNEUMONIA IN CHILDREN

BY LOUIS FISCHER, M.D.

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New York

BRONCHOPNEUMONIA

THIS type of pneumonia is frequently described as catarrhal pneumonia. Because of its anatomical peculiarity in affecting lobules or lobular areas, rather than lobes of the lung, the disease is described as lobular pneumonia. It is this type of pneumonia that is usually met with after the system has been devitalized by the acute infectious disorders. We therefore frequently find bronchopneumonia as a sequel to or a complication of measles, diphtheria, typhoid, or whooping-cough. This type of pneumonia does not terminate in a crisis, but the temperature comes down gradually by lysis. There is no distinct duration or period over which a bronchopneumonia may run. In one child a bronchopneumonia may terminate in two weeks, while in another case with the same form and severity the disease may continue and extend over a period lasting many weeks or months.

Not infrequently the small lobular areas of consolidation will coalesce, forming an inflammatory type resembling the lobar or croupous form of pneumonia. I have frequently seen the inflammatory areas extend, so that we have before us the so-called "wandering type" of pneumonia.

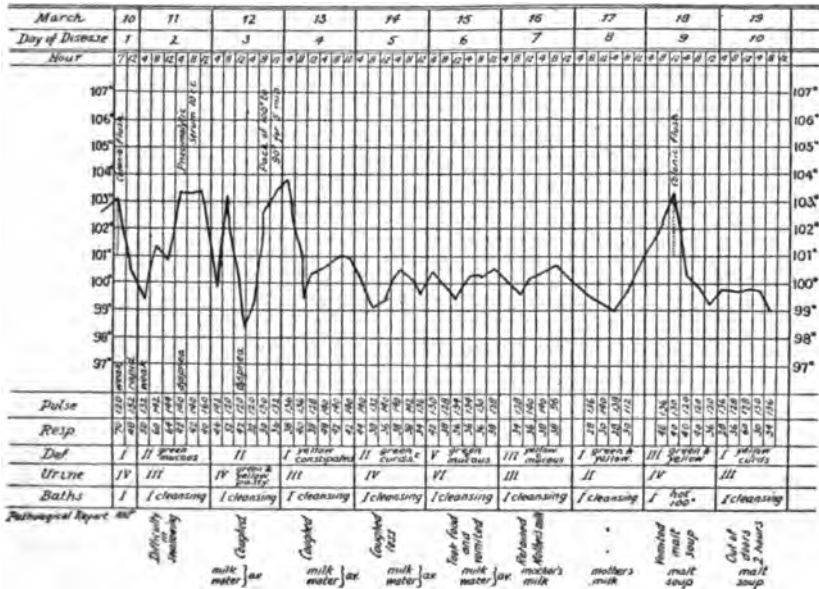
The following case of bronchopneumonia was admitted to my service in the babies' ward of the Sydenham Hospital.

Mary D.,¹ 7 months old, was admitted to the hospital March 10, 1909. She was bottle fed since birth. Had been sick nine days before admission, with fever, chills, and cough; there were no convulsions. She vomited the day of admission for the first

¹ I am indebted to Drs. M. Goldman, I. J. Levy, and S. Littenberg of the Sydenham Hospital Staff, for data in the cases reported.

time. The family history was negative. The past history showed nothing of importance; there were no previous illnesses. Physical examination of the thorax showed marked dulness on percussion at the lower lobes on both sides. There were also subcrepitant râles. March 13, 14, and 15, no change. On March 20 there were dulness and bronchial breathing and friction sounds, on the right side. Crackling râles were also heard on the left side. The abdomen was distended. There was marked evidence of a

CHART I.



rachitic rosary. On March 11, 10 c.c. of a polyvalent pneumolytic serum were injected into the cellular tissue of the abdomen. Before the injection of serum the blood count showed: White blood-corpuscles, 16,100; polynuclear leucocytes, 46 per cent.; lymphocytes, 54 per cent.

Three hours after the injection, the blood count showed: White blood-corpuscles, 17,000; polynuclear leucocytes, 60 per cent.; lymphocytes, 40 per cent.

This case remained in the hospital about two weeks and was then discharged cured.

This type of pneumonia is met with in that class of children offering the least resistance. We must therefore expect this type in children having a rachitic history. In like manner syphilitic children are very prone to this type of bronchopneumonia. If we are dealing with a weakened system, undermined by tuberculous infection, then an additional bronchopneumonia (tuberculous pneumonia) offers little hope for recovery. I have frequently met this type of infection while making my rounds in the diphtheria wards of the Willard Parker Hospital, and it is noteworthy that a large number of cases of diphtheria complicated by this type of bronchopneumonia terminate fatally.

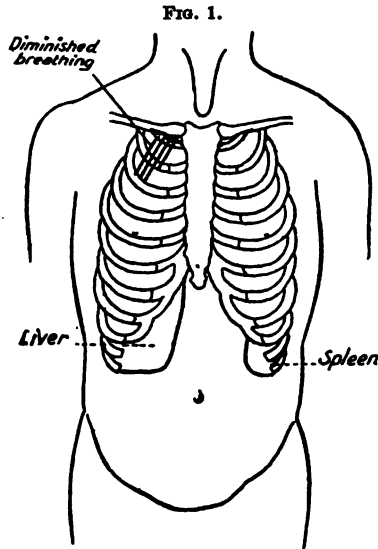
It is hardly in the province of this paper to describe the mode of infection or the specific pathogenic bacteria that bear a causal relation to this disease; suffice it to say that the profound toxæmia caused by the constant filtering into the system of the toxins generated by the micro-organisms paralyzes the vital nerve-centres of the heart, and disturbs the function of the vital organs of the body. It is a noteworthy fact that the glands, such as the peptic glands, do not functionate properly, and their secretion is as a rule inhibited by most of the toxins of the pathogenic bacteria associated with bronchopneumonia.

What has been said concerning the peptic glands applies as well to the function of such important organs as the liver. Equally important is the fact that the kidneys do not perform their physiological function during the course of a severe infection like bronchopneumonia. The toxin, by virtue of its power of permeating all the tissues and organs, saturates the kidneys and destroys, by its action, their power to properly perform their excretory duty; and when excretion of toxins does not take place and the poison is stored in the system, we frequently have an additional complication added to an already severe disease.

The origin of an acute renal congestion and hæmoglobinuria originates from such toxins. In like manner, both nephritis and pyelitis have been seen by me during the course of a severe pneumonia. This added danger militates against a favorable prognosis because organic lesions, even though their acute symptoms subside, may leave focal areas of inflammation, or may terminate in chronic or organic lesions.

From what has been said, we can see that from the very beginning the disease requires most careful observation. The physical signs must be studied and noted day by day. The best results will be attained by him who, mindful of the possible complications, watches for them, and meets every symptom as it arises.

Symptoms and Diagnosis.—The most important symptoms noted are those of a bronchial catarrh or a severe type of bronchitis. Fever is usually present. It is of an irregular type. Some children may have a temperature of 100° F. in the morning and the



evening temperature may range between 103° and 104° F. In another class of cases the temperature may range between 101° and 102° F. in the evening. This type of pneumonia occasionally presents the type known as the "step-ladder" type. The temperature rises from 100° or 101° F., each day rising one degree higher, until the temperature reaches 105° F.

In such a case of bronchopneumonia, it is necessary, when the fever presents similarity to typhoid fever, to note the presence or absence of the gastro-enteric symptoms, the enlarged spleen, and rose-colored spots, before eliminating typhoid fever. The crucial test is the presence of the Widal reaction in the blood, but this is

not present before the end of the first week or the beginning of the second week of typhoid. The respirations are usually increased in frequency. There is also dyspnoea. The difficulty in breathing can best be studied by observing the intercostal spaces and also the epigastrium, which sinks at each inspiration. The *alae nasi* distend with each inspiration. There is an anxious expression of the countenance. Cyanosis affecting the face, the lips, and frequently the nails can be noticed. The respiration is very superficial and labored. It is irregular and very jerky. Some cases may have 44 to 50 respirations per minute, while others may have from 60 to 70 respirations per minute.

Physical Examination.—The physical examination of the thorax shows moist râles, sibilant or sonorous râles, or coarse mucous râles; at times distinct bronchial breathing accompanied by a metallic sound is heard. Percussion will usually show marked areas of dulness. There is also resistance on percussion. Where small areas are affected we must be on the lookout for dulness due to enlarged bronchial glands.

When the disease terminates favorably the temperature falls, the pulse assumes a more regular character; the heart sounds, which formerly were feeble, appear louder, stronger, and rhythmical. The cough will be more frequent, the respiration less frequent and not so superficial. Children who formerly were apathetic now appear to notice everything, and are very sensitive on being handled, and especially so during an examination. The physical signs of a diffuse bronchitis and the diffused areas of moist râles associated with the localized areas of bronchial breathing disappear. The bronchial breathing which existed before now becomes vascular in character. The pulse, which formerly was greatly accelerated, and the respiration, which was very frequent, now both return to their normal state. The whole character of this affection has no specific rule, but drags along without a distinct termination, differing from that condition so well known and described as croupous pneumonia. It is not rare to note in the pulse, respiration, and temperature the signs of an apparent cessation of the inflammatory condition, but to find on examination of the lungs that fresh inflammation has begun.

We can therefore see that a bronchopneumonia frequently continues as an inflammation which spreads from portion to portion

and from lobe to lobe of the lung, and thus devitalizes the system. The symptoms affecting the gastro-intestinal tract and those referred to the genito-urinary organs are the same as are found in croupous pneumonia.

In describing lobar pneumonia, it is usually spoken of as a self-limited disease. I shall speak of this later on. When we consider bronchopneumonia, I would rather speak of it as an unlimited disease. It may last weeks and it is just as likely to persist many months. While many cases have a favorable termination, quite a number end fatally. The reason for this frequent fatality is that the disease runs a protracted course, it undermines the constitution and it is by no means rare to have a tubercular bronchopneumonia follow the primary bronchopneumonia. When suspicion points to the possible development of tuberculosis, then a valuable aid in sustaining the diagnosis of tuberculosis is found in the cutaneous tuberculin reaction.

Cutaneous Tuberculin Reaction.—With the aid of the Von Pirquet scarifier or an ordinary vaccinating lancet, we scarify two small areas. The site chosen is the one ordinarily used for vaccination. In scarifying, care must be taken not to produce a bleeding surface. A drop of tuberculin is then rubbed into one of the scarified areas, the second scarified area is left as a control. No after-treatment is necessary, except that the usual rules of cleanliness should be carried out. After twenty-four hours, or in a tardy reaction after forty-eight hours, in a case of tuberculosis, there is a distinct redness, and in some cases a papular swelling is noticed. If an erythematous redness 10 mm. in width appears, *this should be regarded as a positive reaction, and as indicating the possibility of tuberculosis.* Other tuberculous cases may not give this cutaneous reaction with tuberculin until forty-eight hours after the inoculation has been made. These are known as tardy reactions. Of greater value than this positive reaction is the absence of such reaction, for by it we can, as a rule, exclude tuberculosis.

Treatment.—Children cough, and then swallow the sputum instead of expectorating it. When cough is violent, and the secretion from the bronchi is abundant, then large quantities of purulent material will be swallowed. The elimination of such putrid discharges demands either a laxative such as castor oil or an emetic.

I make it a rule to leave a standing order during my hospital service, to give a teaspoonful or more of castor oil every morning. Viscid secretions in young infants demand emetics. After poulticing for twenty-four hours, I order (for an infant one year old), $\frac{1}{16}$ gr. of apomorphine hypodermically, to be repeated in one hour if no emesis results. A child five years old may receive $\frac{1}{4}$ gr. apomorphine, repeated if necessary to produce emesis. An emetic should never be ordered immediately after feeding or nursing, but rather should it be given one-half to one hour before the next feeding is due.

One word concerning apomorphine. In tablet form apomorphine deteriorates. It should, therefore, always be prescribed in a freshly prepared solution, made from the powder.

Another rapid and valuable emetic is sulphate of copper. This should be given by mouth, in a dose of 1 gr. (0.06 Gm.), dissolved in water, and repeated in one hour if no emesis results from the first dose.

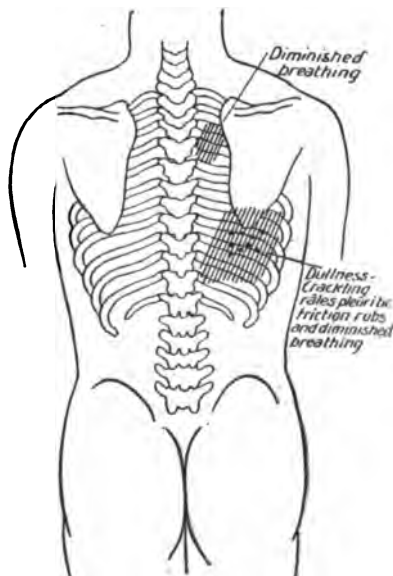
The treatment of a bronchopneumonia consists in relieving symptoms that are urgent, such as cough, dyspnoea, and torpid functions due to glandular inactivity. To relieve cough and loosen viscid secretions during the course of a bronchopneumonia, we must remember steam inhalations, such as twenty drops of beechwood creosote in a pint of steaming water. This can be put in an ordinary croup kettle or a steam atomizer. I am not in favor of placing children with cyanosis or dyspnoea, due to small areas of consolidation, in a tent, thus shutting off oxygen. My plan is to permit a free current of air, but to throw the jet of steam so that the air surrounding the patient is impregnated with this vapor. The frequency of the steam inhalations depends on the urgency of the symptoms. In some cases I order the steam to be used from five to ten minutes, and repeated every hour. Other cases require a more prolonged steam inhalation, say fifteen to twenty minutes in each hour. Besides beechwood creosote I use pine-needle oil (ol. pin. pumil.) in the same dosage as creosote, previously stated. At times I combine pine-needle oil with an equal quantity of compound tincture of benzoin. If cyanosis persists and there is marked evidence of dyspnoea in spite of the steam inhalations just suggested a warm flaxseed poultice, containing ten to twenty

per cent. of powdered mustard, should be applied over the diseased portion of the chest, until local hyperæmia is produced. If the skin is irritated by the use of mustard, we can continue the poulticing by using flaxseed, omitting the mustard, but with the addition of lard. These poultices are to be renewed once every hour, and covered with an oil-silk jacket. The local effect of cupping by applying dry cups to the posterior and anterior portions of the thorax should be remembered. Such cupping should be repeated twice a day, always choosing new places for their application, care being taken not to burn the skin.

LOBAR PNEUMONIA

Sidney G., three and a half years old, was admitted to my service in the babies' ward of the Sydenham Hospital, March 15, 1909. The family history was negative; no tubercular, rheumatic,

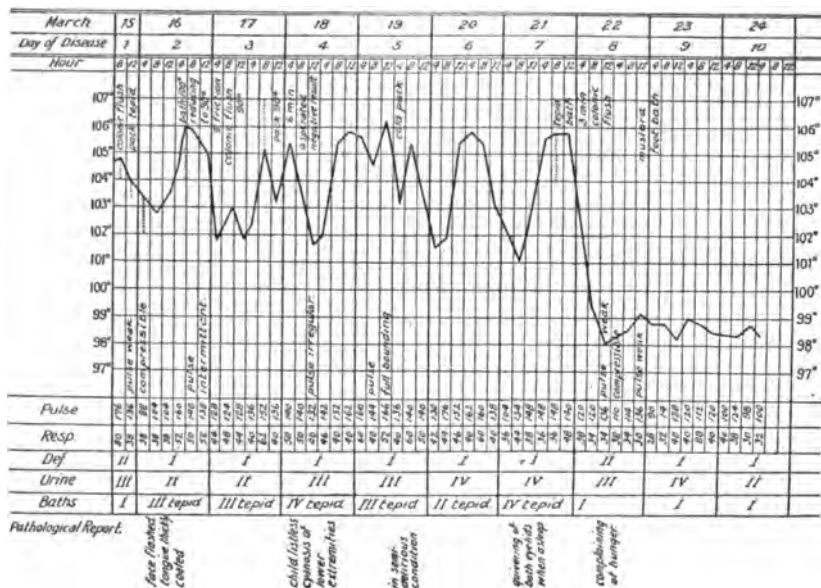
FIG. 2.



or syphilitic history was obtained. Six months ago the child had measles, and three months previous it was necessary to excise some glands from his neck. Whether or not these were cheesy tubercular glands could not be discovered. The present illness began five days

ago with chills, fever, vomiting, and cough. There were no convulsions. The physical examination showed the abdomen distended, the spleen enlarged, the liver border felt three finger-breadths below the costal margin. At the base of the right lung there was dulness on percussion, crackling râles, pleuritic friction sounds, and diminished breathing. During the following two days there was diminished respiratory murmur, heard anteriorly on the

CHART II.



Case of Sidney G—.

right side, and these symptoms were markedly increased until the third day after admission to the hospital; then loud bronchial breathing was audible. The diagnosis of lobar pneumonia was made, and it was evident that the process began in the centre and extended to the periphery. The whole right lung was involved in this process. A study of the temperature, pulse, and respiration chart will show that the temperature ranged between 106° and 102° until the seventh day, when the crisis occurred and it dropped from 105.8° to 98° F. The profound toxæmia caused myocarditis, which at the time of writing has greatly improved. The heart sounds were feeble, the first sound was muffled and weak,

and scarcely audible. The pulse was irregular and intermittent; the rate was irregular and varied from 110 to 80 beats per minute.

There was a heavy trace of albumin in the urine, in addition to a few hyaline casts and pus cells. The urine gave a positive diazo reaction. This same condition was noted for four days, after which time the urine gradually cleared.

The blood count on admission to the hospital showed: White blood-cells, 31,200; polynuclears, 76 per cent.; lymphocytes, 24 per cent. Five days later, on the day of the crisis, the blood count showed: White blood-cells, 14,200; polynuclears, 61 per cent.; lymphocytes, 39 per cent.

This specific infection is caused by the pneumococcus, though in a few instances we may have a lobar pneumonia caused by the invasion of the streptococcus. The infection frequently spreads from an acute streptococcus angina, and for this reason we should always suspect, in cases of simple tonsillitis with persistent high fever, the possibility of an extension of the inflammation through the lymph-channels, giving rise to a pneumonia.

Apex Pneumonia.—In apical pneumonia we frequently find a series of meningeal symptoms. Not infrequently the disease is ushered in by convulsions. Other children have marked rigidity of the sternocleidomastoid muscles. The head is retracted. There is opisthotonos. Rotation of the head, owing to the rigid muscles of the neck, will be impossible and cause pain. Such meningeal symptoms are due to irritation of the cervical ganglion, and are most probably caused by and due to the effect of the toxin on the cerebral centres.

The differential diagnosis between cerebrospinal meningitis and lobar pneumonia depends on the following signs and symptoms: The absence of the *tache cérébrale* in pneumonia; absence of the Kernig symptom; absence of the Babinski reflex; the reaction of the pupils will be normal in pneumonia; lumbar puncture if performed in pneumonia will give a clear watery fluid, if in cerebrospinal meningitis, the fluid will be turbid and contain the *Diplococcus intracellularis*.

The physical signs in the thorax are usually positive. Bronchial breathing is usually heard along with moist râles and the characteristic subcrepitant râles. Besides this, there is marked bron-

chophony. There is a marked resistance on percussion in addition to dullness. The breathing is superficial, shallow, and, owing to the inflammatory condition of the lung, the accessory respiratory muscles are called into play. The *alæ nasi* show the dyspnoea; and the intercostal spaces, if observed, show increased respiratory effort. There is a lack of expansion noticeable which involves the whole of the affected side. The lack of expansion is noticeable in the subclavicular region on the affected side. The early appearance

FIG. 3.

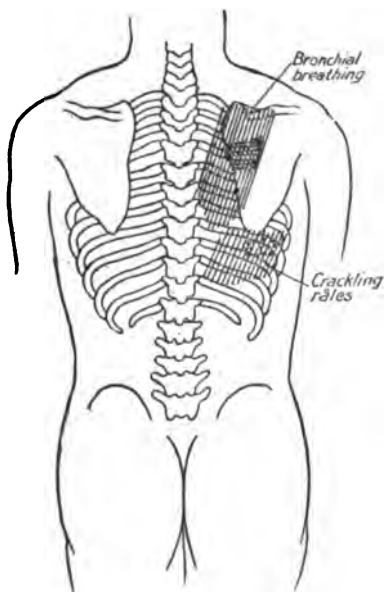
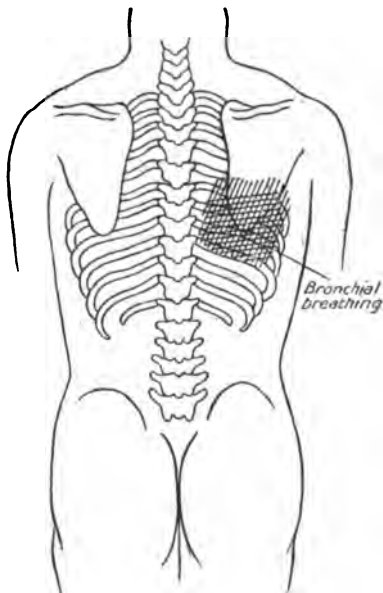


FIG. 4.



of this sign is very important in the diagnosis of lobar pneumonia affecting the centre of the lung, before the physical signs derived from auscultation and percussion can be made out.

Pulse and Respiration.—In lobar pneumonia the normal ratio of pulse and respiration, which is 1:4, or corresponding to 30 respirations to 120 pulse beats, is disturbed. We sometimes find 40, 50, or 60 respirations with 140, 150, or 160 pulse beats. This ratio instead of being 1:4, is frequently 1:3 and at times 1:2. When such disturbances exist along with a temperature of 103° to 105° F. or more, then we should suspect a *central pneumonia*, even

though distinct physical signs on percussion or auscultation are absent. Hypersensitive children, such as rachitic children, usually have temperatures of 105° – 107° F. This disturbance of the thermic centre, plus the toxæmia, is one of the main reasons for the associated initial convulsions or meningeal manifestations. Hyperpyrexia with temperatures of 106° – 107° F. are not necessarily fatal.

The Temperature.—The temperature is higher in the evening, and there is a remission of at least two degrees in the morning. Thus we may have a temperature ranging from 103° in the morning to 105° F. in the evening.

The course of the disease extends over seven to nine days, rarely longer, unless there is an extension of the inflammatory process or a complication. As the disease begins suddenly, so it terminates abruptly, and there is a crisis in which the temperature will drop five to eight degrees. Delirium is frequently present at the time of the crisis.

The Blood.—The examination of the blood shows marked leucocytosis, and this increasing leucocytosis is a very favorable indication. A leucocytosis therefore of 20,000 or higher shows good resistance, whereas a leucocytosis of 9,000 or 10,000 during the height of the febrile process is a grave sign.

In this type of pneumonia we have an increase of the polynuclear cells, which rise sometimes as high as 70 per cent. Normally the polynuclear percentage is rarely above 50 per cent. in children. Eosinophiles disappear during an attack of pneumonia.

The Urine.—During every pneumonia there is usually marked albuminuria due to the febrile process. On account of the frequency of nephritis, it is important to make daily examinations of the urine to detect the beginning of a kidney complication.

Abdominal Distention.—Abdominal distention is frequently found in pneumonia. It is a very distressing symptom. Pain in the abdomen is usually described in older children as occurring in the right inguinal region, if pleurisy or consolidation of the right lower lobe exists. A rule, therefore, is to examine the lung carefully so as to exclude pneumonia in a case pointing to a *probable but not positive appendicitis*. Intestinal paralysis due to the pneumococæmia is a frequent cause of persistent abdominal distention.

I was called to see a child about eight years old, who had a temperature of 105° F., respiration of 48 and pulse of 150, with a history of previous angina. When I saw the case in consultation with Dr. Enton, there was dulness at the apex of the right lung and bronchial breathing. From the continued pyrexia and toxæmia there was delirium. The diagnosis was lobar pneumonia. The consolidation involved the whole of the right lung. On the following day there was a sudden abdominal distention, which seemed to interfere with respiration by pressure on the diaphragm. With the aid of an ox-gall enema considerable flatus and fæces were expelled, and the distention was somewhat reduced. Dr. Willy Meyer was called in consultation. He agreed with me that no surgical condition existed, and that the distention was most probably due to intestinal toxæmia causing local paralysis. This proved to be the case. After the crisis, the distention gradually disappeared and the abdomen returned to its normal size.

Treatment.—Lobar pneumonia is recognized by the New York Board of Health as a communicable disease. Our first duty therefore is to isolate the patient. Next in importance is to use the largest room in the house, with an abundance of fresh air. Admit all the sunlight possible. Keep visitors out. The temperature of the room should be kept between 68° and 70° F., never warmer, rather cooler. Avoid draughts. Do not expose and chill a devitalized child by roof exposure. It may do harm. I know of a death due to such exposure in winter.

Fever Treatment.—There are four methods of eliminating toxins from the body: First, through the skin; second, through the kidneys; third, through the bowels; and fourth, through the lungs. It is important to remember that during every febrile process the glands suffer, hence the secretions are torpid, and the emunctories of the body require stimulation.

To produce diaphoresis one drop of tincture of aconite added to thirty drops of liquor ammonii acetatis can be given every two hours until perspiration results. A two-minute mustard foot bath, at body temperature, will aid in producing diaphoresis.

Some children are sensitive to high fever and may show twitching or convulsions. Older children may have a muttering delirium. Some cases bear high temperatures, others show marked depression

and somnolence. If the skin is hot and red and the temperature 105° F. or over, then a tub bath should be given, at a temperature of 100° F., to which cold water is added until the temperature of the bath is reduced to 90° F. During the bath constant friction should be applied to the chest. If the pulse is good before the bath, then no cardiac stimulant is indicated, but if the pulse is weak, then it is safer to give one-half grain dose of caffeine sodium benzoate or one one-hundredth grain strychnine with ten minims whisky diluted with a little water. These tub baths should only be used for very high temperatures, of 105° or higher. For a temperature ranging between 103° and 105° F., I prefer a tepid pack consisting of a sheet wrung out in water having a temperature of about 85° F. Such tepid packs should be renewed once every few hours, care being taken not to disturb the child in a sound sleep.

Flushing the rectum or colon with one or two pints of cool water, at a temperature of 80° F., is a good means of reducing fever.

Attention to the Bowels.—A dose of one or more teaspoonfuls of castor oil to relieve the intestinal tract is advisable. A very pleasant laxative and one that I use in preference to castor oil, in older children, is citrate of magnesia. It not only has a laxative effect, but a diuretic effect as well. It also quenches thirst. I frequently advise the use of acidulated water, made by adding fifteen (15) drops or more of diluted phosphoric or diluted hydrochloric acid to a tumblerful of sweetened water for older children. The same is to be given *ad libitum*.

As an expectorant, give one drachm of glycerin and repeat every two or three hours. If cough is troublesome give $\frac{1}{16}$ to $\frac{1}{8}$ grain codeine, repeated in three hours. One-half grain of Dover's power every three hours is also valuable.

Nutrition.—This is the most important part of the treatment. Unless the strength is supported by proper feeding we cannot expect to have resolution take place and see the patient recover. The intervals of feeding should be prolonged and the food given well diluted. An infant that received eight ounces of milk before it was taken sick should receive during a pneumonia four ounces of milk and four ounces of water. If this is not well borne, milk should be excluded and whey given in its place. Soup or broth or

strained gruel may be given. Water should be given freely. Milk soured with lactic acid bacilli, so-called acidified milk, is nutritive and easily assimilated.

Influence of Rest.—No greater mistake is made than to disturb constantly a child suffering with pneumonia. To give medicine every hour, night and day, and keep the child awake, is to retard convalescence.

While food is necessary to stimulate subnormal vitality it should be given with due regard to an infant's requirements, and if the heart's action is good it is poor judgment to awaken a sick child to give food or medicine.

Do not give syrups during fever. Most cough mixtures containing syrup are an abomination. They disturb digestion and do not cause viscid secretions to be secreted nor expectorated. Wise is he who remembers that children cough and swallow their secretions, hence the indication is to eliminate with a dose of castor oil repeated twice in twenty-four hours.

Guarding against Complications.—This can be done by daily examinations of the urine. By this means an acute congestion of the kidneys as well as a complicating nephritis can be detected and treated. Scanty urine requires 2-5 grains of diuretin repeated every three or four hours. Sweet spirit of nitre in 10 to 15 minim doses is useful. Dry cupping over the loin may be tried and if beneficial repeated twice a day. The potassium salts, such as the bitartrate, the citrate, or the bicarbonate, in 5-15 grain doses may be tried. Caffeine citrate is not only a good diuretic but is useful to strengthen the heart in one-half grain doses. The infusion of digitalis made from English leaves may be given in doses of 10-20 minims, to a child 2-5 years old, and repeated every three hours. Digitoxin, the active principle of digitalis, is sold in drug stores as "digalen"; it may be given in 1-5 minim doses, and repeated three times a day. It is important in giving digitalis to remember that it has a decided cumulative effect, hence the lowering of the frequency of the pulse with higher tension should be the indication as to when digitalis or its preparations should be discontinued.

Theocin is a valuable diuretic in doses of 2-5 grains repeated every three to four hours. This drug was recommended to me

through the kindness of Prof. Adolf Baginsky, while making rounds with him at the children's hospital in Berlin.

Cardiac Complications.—At the slightest failing of the pulse, showing cardiac weakness, we should suspect the beginning of myocardial insufficiency. A pulse of low tension that is irregular or intermitting requires strychnine. Frequently strychnine combined with whisky produces good results. Beginning with 1/100 grain, gradually increase the doses until 1/60 grain is given, and repeat the dose several times a day. It is self-understood that the toxic symptoms of strychnine, such as muscular twitching, must be guarded against, and the drug stopped immediately when such symptoms are noticed. Gentle massage given twice a day is useful to stimulate the circulation.

Every case of pneumonia must be carefully studied and individual idiosyncrasies noted. The dose of a drug that produces the desired effect rather than the physiological dose should be given. Some children respond easily, hence the rule should be to begin with the minimum dose and gradually increase until it is effectual.

Water.—In febrile conditions it is important to order water. Cool water with or without lemon juice or orange juice is required. Water aids in the elimination of food.

Concerning Antipyretics.—All fever drugs are cardiac depressants. I do not use them, either in hospital or private practice. I find the therapeutic results are far better comparatively when the above-outlined plan of treatment is carried out.

PSYCHASTHENIA *

BY BRADFORD C. LOVELAND, M.D.

Neurologist to the Hospital of the Good Shepherd, Syracuse, N. Y.

It is a difficult thing to find a name which gives an adequate conception of the malady it represents, but if this were not the case a description would be unnecessary.

The name which forms the title of this paper is an example of one which expresses only one prominent symptom of the disorder.

A very readable paper on the subject of psychasthenia, with the report of a characteristic case, by Dr. Joseph Collins, appeared in the *New York Medical Journal* of Feb. 15, 1908.

The name was first applied by Dr. Janet of Paris to certain cases of the neurasthenic type characterized by obsessions, fears, doubts, psychalgia or depression, mental anguish, uncontrollable movements, enfeebled will power, and more or less of the physical signs of neurasthenia. The neurasthenia group is thus being diminished, if not decimated, by a closer diagnosis, as hysteria, dementia præcox, arteriosclerosis affecting the nervous system, etc., are being subtracted from it. So the condition now known as psychasthenia is not new, but until comparatively recently has been included in that ill-defined and worse understood group of cases termed "neurasthenia."

Those, however, who studied neurasthenia with sufficient care were accustomed to divide it into smaller groups according as its principal symptoms were cerebral, gastric, sexual, or emotional; so we read in medical literature of gastric neurasthenia, sexual neurasthenia, etc., the emotional type being usually called hysteria, or said to be complicated with hysteria. The cerebral and emotional types being often confounded are considered to belong to the hysteric class.

The word psychasthenia means brain exhaustion or brain weakness; but mere brain fag has no relation to the condition I am about to describe, and which has been given that name. Besides the group

* Read before the Onondaga Medical Society, Feb. 8, 1909.

of symptoms enumerated from Dr. Janet's description there is also psychalgia or mind pain; and not infrequently such an intense concentration on the troublesome obsessions that the thoughts are projected into the environment, as it were, and the patient is the subject of hallucinations of hearing or sight, which, like other symptoms, he may for a time be able to disregard by the help of his reason and will power. In fact the cases referred to are not simply exhausted mentally, and in some there has been no reason for brain exhaustion, as one of my cases was a farmer, doing what work he did with his hands in the open air, and almost no real mental work unless the worry and anxiety he expended on his condition could be called such.

Dr. Janet makes six divisions or clinical varieties of psychasthenia. (1) The doubters. (2) The scrupulous, with obsessions of a moral nature. For instance, such a patient making a general statement regarding a date would be driven to the utmost exactness, even to the hour and minute, by his conscientious scruples. (3) The criminal. They rarely yield to the criminal impulse, but have that mental trend. (4) Inebriates, dypsomaniacs, drug *habitués*. These show the least resistance to the dominant idea. (5) The genesically perverted. (6) Those associated with delirium.

Each of these classes has its counterpart among the paranoiacs; but these latter have not sufficient reason and will to control the obsession, and hence it dictates their actions. The points in common in the psychasthenics are the obsession, or dominant idea, the fears, lack of self-confidence, mental anguish, depression, often involuntary muscular twitching, occasional hallucinations of sight or hearing, the obsession being the root from which the other mental symptoms spring. Recognizing these to be abnormal the patients are at first and frequently for some time able to overcome or disregard them by the aid of reason and will power; but sooner or later they will consult a physician, unloading their fears and anxieties on him, and by his explanations and advice they may be able again to get the mastery over the dominant idea.

The hallucinations, which the patients recognize as such, are especial causes of mental anxiety, often completely unfitting the patient for work, and driving him to the point of distraction for fear he is going insane. It often happens that those not versed

in the peculiarities of mental disease are ready to regard such hallucinations as indicative of insanity, but we know that no one symptom is pathognomonic of insanity any more than one symptom alone will serve to diagnose scarlet fever. Intelligence is not disturbed, and the patient often describes his condition with such a degree of distinctness as one might do in describing the symptoms of another person; and not infrequently the patient will feel as if he was not himself, a feeling of dissociated personality. These symptoms naturally cause lack of self-confidence, fear, mental anxiety, melancholy, etc., to a distressing degree.

The causes of this condition begin with heredity, continue with environment and end with causes of nervous wear and tear, some of which may be removed. Many of these patients are the offspring of nervous parents, though we find the type of nervous disease changes from generation to generation; and the nervous environment is equally important in its influence, for a proper environment may correct much of the evil of nervous heredity.

Of the cases which I shall report one had a very nervous mother, another had a nervous mother who also suffered with bronchitis, and the third was the son of farmer parents who were both nervous but not invalids.

One thing about the environment worth mentioning is that in two of the cases mentioned the patients suffered from a "little knowledge." Two of the three cases considered in this paper had hallucinations, one of vision, the other of hearing.

Three cases, each characteristic in its way, will serve as illustrations.

CASE I.—Miss A. C. was referred to me on April 15, 1907. She was 31 years of age, and had been variously occupied as book-keeper, stenographer, and teacher. Her father died at 72, having been more or less an invalid with rheumatism. Her mother was alive but in poor health from nervous and bronchial trouble. She had one sister, one half-brother, and one half-sister, all well. She had measles when a child, diphtheria at 14, and was out of school for a year and a half for menstrual difficulties. At the age of 25 she was taking French lessons, and for a time did *very well*, and noticed that she could often anticipate the question the teacher was about to ask her, and always had the answer ready. About this

time during one of her recitations she answered a question asked her, and either had or thought she had a spell of temporary unconsciousness, which must have been only momentary at most and was not noticed by other members of the class. In this spell she thought she had in some way done something which compromised her sex, and that in relation to her teacher, which in turn caused her the greatest chagrin and distress. From this time she found that she could not concentrate her mind on her lessons as before, but when in the presence of her teacher began to have a peculiar sexual excitement, and to feel that she was in some way under his power. Now she became much distressed in mind and depressed. She came across a book by Dr. S. Wier Mitchell from which she got some ideas on hypnotism (the little knowledge referred to) and came to believe she was under the hypnotic influence of the teacher. This preyed more and more on her mind till she feared to pass him on the street, and would go around a block any time to avoid meeting him. As this sense of being under some hypnotic influence increased she began to hear voices, particularly in the morning on waking, or when tired at night and attempting to sleep, which she attributed to the supposed hypnotic influence. These voices became more frequent till they troubled her at any time when she was not occupied with absorbing work.

The voices made jeering remarks to her, often taking thoughts which were in her mind and expressing them in a way to make them ridiculous. She soon was unable to keep her mind on her work, and after trying various means for relief consulted Dr. Juliet Hanchett to assure herself that there was no disease of the pelvic organs needing attention. She was found normal in this regard, and after she had told her story she was referred to me.

The treatment will not be discussed till after the other case reports, but I will say that she went back to work in a few days, and has worked practically ever since. Last summer while still holding her position as stenographer and bookkeeper she finished her study and completed her examinations for a State teacher's certificate, and is teaching school this winter. She writes that she is doing well and enjoying her work.

CASE II.—Miss M. H., 30 years of age, came under observation July 22, 1906. Occupation: student, housework, and teacher of

physical culture. Her mother is a very nervous woman but not an invalid. Father well. One sister and one brother, both well. She has always been nervous, and could not complete her college studies as her brother and sister did.

Present trouble began with exhaustion about eighteen months before she consulted me. She had what she called nervous spasms, and every variety of hysterical symptoms. She was very much troubled about sleep, and was obliged to take some hypnotic for about a year before she came under my observation. She used veronal on a prescription from her physician for some months, but became alarmed at a stupid, drugged feeling which followed sometimes for days after its use, and stopped it. When trying to go to sleep she would, to use her own expression, "see everything hellish." She could control these "visions" in the day, but at night she was driven almost distracted by a panorama of horrible moving objects, grotesque, impossible. Effigies of men and animals, of absurdly horrible proportions, would chase each other past her vision till sleep was out of the question. She also had a roaring in her ears which added to her troubles. She had more or less backache, and some dysuria; but these were secondary to her mental suffering, which made her fear she would become demented. Her physical condition showed a fairly nourished body, height 5ft. 4 in., weighing 105 lbs., some sensitiveness over the liver, stomach prolapsed to the level of the umbilicus, nephroptosis on right side, uterus retroverted, knee reflexes exaggerated, other reflexes normal.

I sent her to an oculist, who reported astigmatism, and also muscular imbalance in two directions, outward and downward. He fitted glasses, and suggested tenotomy for the muscular trouble, which I encouraged but to which I could not secure her consent. She later tried another oculist who attempted to correct the muscular trouble by exercise with prisms, but he finally gave it up. A gynecologist also was consulted and advised an operation for ventral fixation, but this was never done.

The patient made a practical recovery, as she is able to attend to her usual duties, including her Sunday-school work, to sleep at night without hypnotics, to walk a good deal, and feels herself in pretty good condition even if she does still have some backache or distress in the bladder.

The last weight I have recorded was 115 lbs., on Dec. 17, 1908, when she called on account of a slight attack of diarrhoea.

CASE III.—Mr. W. H. W. was referred to me on Dec. 11, 1906, by Dr. Halsey of Ellisburg. He was 29 years of age, a farmer by occupation, parents both alive, nervous, but not invalids. One cousin had an attack of depression (probably melancholia), but recovered. Patient has had measles, mumps, whooping-cough, and chickenpox. He was full grown at 16 years. In 1901 he had an attack of depression which lasted about six months, and in 1903 another similar attack of about the same duration. In Dec., 1905, after a usual day, depression came on suddenly, and he has not been well since. He had an attack of jaundice since the present trouble began. Appetite is good and he is a hearty eater. With the beginning of this attack he began to have a constant worry about his sexual apparatus—no lack of sexual power, but a constant doubt whether he was correctly formed or not. He was the father of one child nine months old at that time. His worry could not be relieved by any reassurance from his physician, and soon he began to think over the comparative anatomy of the sexual organs of the animals he was caring for.

Later he began to be annoyed with thoughts doubting the loyalty of his wife; though he admitted freely there was no reason for it, and blamed himself for allowing such thoughts to enter his mind, still they would come, and it bothered him to have the hired man stay in the house at night. The principal obsession seemed to be his doubt of his own sexual normality, and from this the other distressing symptoms grew. This was the condition when he consulted me. After careful examination I found him organically sound; but he could not get his mind away from the contemplation of his sexual organs, or the comparisons he had been making between man and animals, though he told me he knew it was all wrong to think this way, and he believed Dr. Halsey and me when we told him he was sound; still the thoughts would come back, and he wanted a certificate written out that he could refer to. He also feared to touch his sexual organs after milking cows or doing other farm work lest he should leave some permanent contamination, and asked me if it was possible to damage himself in this way. I found his vision far from normal, and Dr. Marlow fitted him with

glasses, and later did two tenotomies, which I am sure was a great benefit to him.

His recovery has been slow, with ups and downs, but my last notes on Oct. 6, 1908 say, "Pretty well. Still has some worries, but is able to reason them away."

The treatment of these cases comes well within the realm of psychic therapeutics, but any possible sources of unnecessary nervous irritation must not be overlooked.

In Case I the treatment was almost entirely psychic, a few nux-vomica and asafoetida pills being all the medicine prescribed.

For the successful application of the psychic method to these cases the complete confidence of the patient must be secured as a foundation step. It may be said that a patient would not consult a physician in whom he had no confidence; but the confidence which prompts the patient to consult a physician may be very little, only a desire to get his opinion, which does not mean much; and unless that little can be developed into a thorough confidence based on the conviction in the patient's mind that the physician *knows* the case, his efforts at psychic or suggestive therapy will fail utterly.

Time must be taken to hear the case as it appears to the patient, no matter how quickly the physician may have formed his conclusion, and no matter how tedious the patient's narration may be. The only way to cut short this necessity is, when the case is clear to the physician and he is sufficiently familiar with its symptoms to warrant the experiment, to venture on the territory of the quack and tell the patient his symptoms after the patient has given him the lead. This is at best a doubtful expedient, and requires great tact as well as broad experience to make it work.

Next, take time to make a thorough and careful examination, even if you have to convince the patient of its necessity by explaining the close relation between the physical processes and the nervous sensations. Then find an explanation of the nervous sensations in physical condition as far as possible, and those that are solely an evolution of the mind must be explained along psychological lines. To accomplish this to such an extent as will give a common ground or understanding between patient and physician may take an hour or two, but it lays the foundation for therapeutic effort. In this work there is no place for the idea which seems to be entertained

by some physicians: "It is only nervous and any old explanation will do." Strict candor and honesty is not only the best policy but is absolutely demanded.

The patient's idea of his trouble being uprooted, and the physician's explanation planted in its place, the next step is to allay the anxiety that such mysterious symptoms have caused in the patient, encourage him to give no heed to his feelings, and occupy his mind with other and more useful thoughts.

The immediate result may in some cases be little less than marvelous, as in Case I, who went back to work almost at once; or it may be necessary to go over the ground repeatedly, both to re-establish confidence and to uproot some new phase of the controlling idea, as was necessary in Cases II and III. In these also I feel sure that the irritation of astigmatism and muscular imbalance were important factors. Even if Case II never completed her eye treatment she gained much from the correction of her astigmatism.

The positive assertion of the facts in a given case often repeated will have a great influence in strengthening the patient's judgment and will.

As to the future prospects for such cases it may be said that as they occur in those of rather unstable equilibrium some nervous trouble is liable to come on again unless they are able to be shielded from unusual strain; but with care in this direction the patient may live a useful and comfortable life. This is essentially the case when the patient may be so convinced of his susceptibility to the domination of the psychic over the physical that he will be able to recognize purely nervous sensations when they arise and disregard them, or at least only allow them their proper place.

Medicine

TUBERCULOUS SEROFIBRINOUS PLEURISY AND ITS TREATMENT *

BY HERMAN B. ALLYN, M.D.

PHILADELPHIA

THE occurrence in my service of fourteen cases of pleurisy has aroused fresh interest in a subject that has always attracted me. Of these cases six were instances of serofibrinous pleurisy. Two cases were instances of chronic adhesive pleuritis, in which the layers of the pleura had become thickened and adherent; in one, however, there was also some fluid, as ascertained by aspiration. Five cases were instances of acute plastic pleurisy, two of them in connection with pneumonia, one with typhoid. One proved to be a case of lymphosarcoma of the pleura.

We do not yet know enough about all the causes to classify all cases of pleurisy satisfactorily, but we can say that pleurisy may accompany any of the acute infectious diseases—scarlet fever, measles, typhoid, erysipelas, rheumatism, septicæmia, pneumonia, and tuberculosis. The germs that are found most frequently are the tubercle bacillus, pneumococcus, and streptococcus. Some cases of pleurisy also are traumatic, and some are due to Bright's disease, new growths, cancer, and sarcoma.

As the whole subject of pleurisy is too vast for discussion, I wish to take up especially serofibrinous pleurisy and particularly that form which is tuberculous.

The disease sets in rather suddenly with chilliness, fever, pain in the side, and cough. There is frequently antedating the attack a history of a cold, or of exposure to cold and wet. The rise in temperature is more gradual than that of pneumonia; the fever does not usually rise as high, not often over 102°. It is not un-

* A Clinical Lecture delivered at the Philadelphia General Hospital, March 6, 1909.

common in our hospital to find patients with well-marked pleurisy, particularly in the stage of effusion, with very little rise in temperature, sometimes with a normal temperature. But this is because the process has lasted some time before the patient came into the hospital and has gradually become afebrile, or because his age and general feebleness have lessened his reactive power. Whatever the explanation, one can usually note a decided difference in the amount of fever when the lung is involved and when the pleura alone is the seat of inflammation.

Pain and cough are the prominent symptoms. The cough is most distressing. It is frequent, dry, and may cause agonizing pain. I have seen patients grasp the affected side with both hands and endeavor to restrict its motion and lessen cough. They learn to take shallow breaths, to avoid talking and motion. Both pain and cough are due to the rubbing together of the inflamed surfaces of the pleura. Usually the pleurisy involves the nipple region or the lower axilla, but it may be found at the bases posteriorly or at the apices. Often the area involved in a plastic pleurisy is very small, sometimes only an inch or two in diameter. Its seat is almost always exactly indicated by the position of greatest pain and tenderness. When the diaphragmatic layer is involved, however, there may be abdominal pain, pain over one kidney, or in the epigastrium with hiccough as a symptom. Serum is poured out at a variable time after the onset of the pleurisy. It may occur almost at once, so that a plastic stage is hard to make out; or its appearance may be delayed several weeks. Usually it can be detected within four to seven days from the onset. After the appearance of the serous exudate the symptoms will depend partly upon the volume of fluid and partly upon the extent and amount of the plastic exudate. Usually the fever, pain, and cough begin to lessen. But if the plastic exudate is extensive and the volume of fluid small, all symptoms will be more severe. On the other hand, if the volume of fluid is great, dyspnoea becomes a prominent symptom, cough being brought on by change of posture.

Usually the dyspnoea is proportional to the volume of fluid present in the pleura, but this is not invariably the case. I have seen a man with the pleura full to the clavicle, and yet not suffering greatly with dyspnoea. The rapidity with which the fluid is

poured out is doubtless a factor. If a large effusion occurs with great rapidity, there will naturally be more dyspnœa; whereas even a larger amount occurring gradually will be better borne.

DIAGNOSIS

The subjective symptoms of a serofibrinous pleurisy are not characteristic. We must look to the physical signs for a positive diagnosis.

Inspection.—Inspection will often reveal lessened respiratory motion of the affected side; but I must say that I have often been surprised at the slight effect of a moderately large effusion in impairing motion, especially when the patient is lying down, and the view is only of the anterior portion of the chest. If the patient is seated a deficiency in expansion at the base of the affected side is usually to be seen. In this position, also, in large effusions, the greater width between the scapula and the spine on the affected side is noted—a sign that Musser lays stress on. The cardiac impulse may be visibly displaced, beating in large, right-sided effusions in the anterior axillary line and in left-sided effusions beneath the sternum or to the right of the sternum. Litten's diaphragm phenomenon may also be absent. The interspaces may appear fuller and the entire side larger on the affected side, or, to state it in another way, the ribs may not show as distinctly as on the sound side.

Greene¹ has called attention to rhythmic lateral pulsation of the heart as a sign of unilateral pleural exudate. The heart moves toward the affected side in inspiration and away from it in expiration, the extent of motion often amounting to two inches. It may be measured by fluoroscopic examination or by auscultatory percussion. It is most marked in medium-sized effusions.

Palpation.—Palpation determines more accurately than inspection the fulness of interspaces, the position of cardiac impulse, and the lessened respiratory excursion upon the affected side. There is rarely œdema in serofibrinous exudates, though it is occasionally met with in purulent exudates. Fluctuation I have never felt. Palpation also detects the presence or absence of tactile fremitus, a most valuable sign. The fremitus is usually greatly diminished or

¹ C. L. Greene: *Amer. Jour. Med. Sci.*, March, 1906.

absent, not invariably, however. Much depends upon the degree of compression of the lung, upon the patulousness of the bronchial tubes, upon the strength and quality of the voice, and perhaps upon the tension of the large bronchi and the presence or absence of bands of pleural adhesions along which the vibrations of the voice may travel. Probably the two most important factors in the transmission of voice vibrations are the strength and quality of the voice and the patulousness of the bronchial tubes. I have frequently found the tactile fremitus preserved upon the side of the exudate, but greatly diminished as compared with the other side if that was sound. I do not recollect any case of serous exudate in which the fremitus was increased or even present in such intensity as to embarrass one in diagnosis, but I have met with empyemata in which that was true. Osler states that in children there may be much effusion with retention of fremitus.

Mensuration.—Careful measurement of the two sides, especially with lead tape, will generally show that the affected side is larger and moves less in respiration. One needs to remember, however, that the right side is normally larger than the left in right-handed persons.

Percussion.—Percussion yields some of the characteristic phenomena of fluid in the pleural sac. Over the fluid the note is usually flat. Sometimes it is only dull, but in the vast majority of cases it is flat. Accompanying the flat note the pleximeter finger, *i.e.*, the one applied to the chest, perceives much greater resistance than upon the sound side, or even greater than that obtained over solidified lung. These two signs, flat note and greatly increased resistance, are almost always present; but as one percusses from the base to the apex he reaches a level where the note first becomes dull and the resistance less, and a shade above this he encounters resonance. It is good practice for the student to pass from resonance to flatness above and below the level of an effusion. It not only trains the ear to perceive differences in sound, but it trains the finger to detect differences in resistance. Above the level of the effusion the percussion note is often hyperresonant—Skodaic resonance—due probably to a relaxed condition of the lungs.

It might be supposed that in pleural effusions the upper level of flatness would be at the same height front, back, and in the

axilla, but it is not so. Usually it is lower at the spine than at the axilla, and about the same height at the sternum as in the axilla. The explanation is a problem in hydrostatics affecting a cone-shaped elastic body. The difficulty is to understand why the axillary portion of the lung should be displaced more readily by fluid.

A much more important sign is *change of the upper level of flatness on change of posture*. This is an infallible sign of fluid in the pleural sac, but it is not always obtainable. It fails when the entire pleural sac is full up to the clavicle; it may not be demonstrable when the volume of exudate is very small; and when the exudate is of moderate or large size we cannot always obtain the sign, because the lung may not be freely movable owing to bands of adhesion. After the position of the patient has been changed a few moments should be allowed for the change to affect the fluid in the chest. I have rarely seen more than two finger-breadths of difference between the upper levels when the patient is lying down and when he is sitting up.

Displacement of Organs.—This is also a most valuable sign. Unlike the sign just mentioned its presence depends upon the volume of fluid present. In small exudates there is usually no displacement recognizable; whereas in very large exudates the heart may beat to the right of the sternum, and the liver or spleen descend an inch or more below the costal margin.

The Paravertebral Triangle of Dulness (Grocco's Sign).—When the exudate reaches to or above the angle of the scapula behind and to the third or fourth rib in front, an area of dulness will also be demonstrable upon the opposite side. This area of dulness is triangular in outline extending from the spines of the vertebræ at the upper level of the exudate in an oblique manner to the base of the lung on the sound side, the base of the triangle extending a variable distance from the vertebræ towards the axilla of the sound side. The base of the triangle is not generally over one to three inches in length. The patient must be in a sitting posture when the examination is made. If the sign is present and is due to fluid, it should disappear or at least the area of flatness become much smaller when the patient lies upon the side on which he has a pleural exudate. It appears to be due to the displacement by the

fluid of the posterior mediastinum to the opposite side. It may be due to such stretching of the pleura that the lower part, when the patient is upright, reaches to the opposite side.

It is noteworthy that Osler says, in speaking of the position of the apex beat in pleural exudates, that there is no rotation of the heart but rather a definite dislocation of the mediastinum with the heart to the right. He says also that in very copious exudation the dullness may reach the clavicle and even extend beyond the sternal margin of the opposite side.

I have found this sign very valuable. It has been present in every case of serofibrinous pleural exudate which I have examined in the past two years. In one case the history and other physical signs indicated rather extensive plastic exudate; but Grocco's sign was present and serum was obtained by aspiration. I have therefore come to regard this sign, and movable dullness and displacement of organs, as the three most trustworthy signs of fluid in the pleural sac. The other signs mentioned may be found under some conditions when fluid is not present; these three taken together infallibly point to fluid in the pleural cavity. Of course in every doubtful case it is not only proper but is a duty to introduce an aspirating needle in order to ascertain the presence of fluid and its character. This method of examination is especially valuable in loculated pleurisy, in small empyemata, and in interlobular empyemata and abscess of the lung. I have never known it to do any harm. In large or medium-sized exudates whether of serum or pus one can almost always make a diagnosis without the aid of the needle, but that is not true of small collections.

ETIOLOGY

The older students of pleurisy would have been compelled to stop with the determination of the presence or absence of fluid in the pleural sac, and its kind. Thanks to modern laboratory methods we can now go further and ascertain the cause of the pleurisy, knowing that the same effect may be produced by a variety of causes. I will limit myself to tuberculous pleurisy.

The tubercle bacillus is the cause of pleurisy in from 40 to 60 per cent. of all cases. This statement is based partly upon the subsequent history of a large number of cases observed as to the

ailments the patients have or the diseases of which they may have died after a period of years. Thus Bowditch reported that in ninety cases of acute pleurisy observed between 1849 and 1879, thirty-two died of or had tuberculosis. Out of 130 cases of pleurisy with effusion observed by Hedges for seven years, 40 per cent. became tuberculous. Of 300 cases of uncomplicated pleural effusion reported by R. C. Cabot from the Massachusetts General Hospital, out of 221 the histories of which could be obtained, 177 after five years had died of or had phthisis. Osler's statistics are to the same purpose. It will be noted that the proportion of tuberculous cases is greater in uncomplicated pleurisies than in those with effusion. This has led some authors to divide pleurisies into two groups, the tuberculous and the non-tuberculous, and to regard as tuberculous all those for which no other cause can be found.

Another reason for regarding many cases of pleurisy as tuberculous is the frequent association of tuberculosis elsewhere with pleurisy. This is true both at autopsy and during life. One finds tuberculosis at one apex followed by pleurisy of the opposite side, or tuberculous peritonitis followed by pleurisy, or disease of the joints with the same sequence.

Some laboratory methods of examination are of great value. It has been ascertained that in the great majority of tuberculous sero-fibrinous pleurisies there is a high percentage of small lymphocytes, ranging from 70 to 90 per cent. Transudates also show a very high percentage of lymphocytes, but they can be distinguished from exudates by the lower specific gravity (1008 or below) and by their lower albumin and fibrin content.²

In the early stage of tuberculous exudates, however, the polymorphonuclear leucocytes may be in preponderance; on the other hand, an excess of small lymphocytes does not prove the tuberculous origin of the pleurisy. I have seen it in sarcoma, and in the ascites of cirrhosis of the liver, where no tuberculous lesion was found at autopsy. It is, like most other signs, valuable but not infallible.

For many years it was only with the greatest difficulty that investigators were able to demonstrate tubercle bacilli in the

² See papers by Percy Musgrave, *Boston Med. and Surg. Journal*, vol. cli, No. 12, Sept. 22, 1904, p. 317, and Herbert S. Carter, *Med. News*, N. Y., Oct., 1904.

exudate. This is explained by the small number of bacilli and by the imperfect technic of the investigators. A few years ago Jos-suet devised an improved method which he called inoscopy. According to this method the serum withdrawn by aspiration is allowed to clot, the bacilli being then caught by the filaments of fibrin. The clot is then turned out upon sterile cheese-cloth and digested in a mixture of pepsin 2 Gm., glycerin and HCl each 10 c.c., sodium fluoride 3 Gm., and water sufficient to make 1000 c.c. After digestion the fluid is centrifugated and the sediment stained for tubercle bacilli. The majority of the bacilli are said to be shorter and broader than the bacilli found in sputum.

A still more exact method of demonstrating the tuberculous origin of the pleurisies is by inoculation of the pleural fluid into guinea-pigs. Eichhorst has shown that in many cases at least 15 c.c. must be used to obtain positive results. Where this is done he showed the tuberculous origin of 62 per cent. of all cases. The tuberculous like other exudates has a high specific gravity, in Carter's cases an average of 1017.9, with a high fibrin and albumin content. It may be serosanguinolent or even bloody.

Of recent years in the Philadelphia Hospital Dr. Rosenberger, Chief of the Clinical Laboratory, has examined the fæces of many tuberculous cases, and of many suspected of being tuberculous. He has demonstrated that practically in all cases of tuberculosis, affecting no matter what part of the body, tubercle bacilli are found in the fæces. Hence his method of examining the fæces has become an accepted part of our diagnostic methods. He has still more recently found tubercle bacilli in the blood. So that a number of cases that hitherto had been doubtful we are now able to declare distinctly as tuberculous.

I have said nothing about the tuberculin test as yet. It seems to me that in most of the cases we can make a diagnosis without it, and that we are not justified in employing tuberculin if we can avoid it. The older method of injection has been largely superseded by the eye test introduced by Calmette, and by the skin test. In the eye test a drop of one per cent. solution in normal salt solution is instilled into the eye, the other eye being used as a control. In the majority of tuberculous cases a more or less active conjunctivitis is set up in from three to twelve hours. In some cases the inflamma-

tion has been so active as seriously to injure the eye, and personally I fear to use it. In the skin test the tuberculin is incorporated with a salve and rubbed into the skin, an efflorescence resulting in tuberculous subjects. It is the safer of the two methods but as yet has not been employed often enough to have an assured place in diagnosis.*

TREATMENT

There are three symptoms which especially call for treatment, namely pain, cough, and dyspnoea.

Pain.—Pain is variable in its intensity. Sometimes it is relatively slight and may be relieved by a hot-water or ice bag, an application of tincture of iodine to the skin, or a turpentine stupe. In severe cases mustard poultices, sinapisms, stupes, blisters, cups, and leeches have been employed. Personally I believe that applications which break the skin or make it very tender are objectionable for two reasons, they open the way to infection and they make the skin so sensitive that soon all local applications must be discontinued, though the pain of the pleurisy may persist. Moreover, they are not as effective in relieving pain as is strapping with adhesive plaster. The skin of the chest must first be washed with soap and water and then sponged off with alcohol. Zinc oxide adhesive plaster, in strips one inch wide, should be used. One end should be fastened a little beyond the spine on the sound side below the seat of pain. While the patient's chest is in full expiration the plaster should be drawn tightly around the chest and fastened just beyond the mid-sternal line. In this way strip after strip of adhesive plaster is applied from below upward until the seat of greatest pain is covered. An ice bag or hot-water bag may also be applied over the seat of pain without disturbing the plaster. When properly applied in full expiration of the chest considerable fixation of the affected side is secured, and with it of course much less friction of the inflamed pleural surfaces, with great relief to the pain. The method may not be applicable when the mammæ are large, and I have never tried to use it in the rare cases when the pain was at the apices of the chest. The plaster may be allowed to stay on for a week or two, until it loosens or the patient becomes uncomfortable from it. It is rarely necessary to reapply it. When sufficient

*See papers by Smithies and Walker, Evans, Engelback and Shankland, and the discussion on them in Jour. Amer. Med. Assoc., No. 50, Jan. 2, 1909.

relief is not obtained from the plaster dressing with ice or heat applied in addition, some anodyne is necessary. The best is morphine hypodermically; a sixteenth or an eighth of a grain once or twice a day may be sufficient. In case hypodermic medication is for any reason undesirable, I prefer to give codeine in quarter-grain doses by the mouth, as it is less apt to cause nausea and constipation. The salicylates are also valuable agents in relieving the pain of a pleurisy.

Cough is relieved by strapping the chest. When other agents are required morphine or codeine may be used hypodermically or by the mouth. Dionin is to be preferred to heroin as less toxic. Codeine with terpin hydrate may be used if there is an associated bronchitis. Some years ago H. C. Wood recommended as a useful cough mixture the following combination: Chloroformi, ℥ xxx, Tr. Opii Camph., Glycerini, Spir. Vini Gall., āā, fʒ i. Dose: a teaspoonful in a little water as often as needed for cough.

When there is any catarrhal condition of the nose, throat, larynx, or windpipe, it should be treated with appropriate sprays and inhalations just as when it occurs independently of pleurisy. Attention should also be bestowed upon the heart; a leaking mitral valve or a weak myocardium may be an important factor in keeping up a cough. All movements should be slow and careful so as to disturb the patient as little as possible. Finally an adequate movement of the bowels and the passage of a sufficient volume of urine will help to lessen cough.

Dyspnœa.—As the dyspnœa, aside from the influence of a weak heart or diseased kidneys, is due to the fluid exudate, the treatment of dyspnœa is essentially that of the fluid exudate. Generally the degree of dyspnœa will depend upon the volume of fluid which is present, and upon the rapidity with which it has been poured out. If the fluid is pus it should be removed at once. Generally aspiration is not sufficient and should not be recommended. But when the patient refuses a more formal operation, aspiration followed by the injection of a two per cent. solution of formalin in glycerin, as recommended by John B. Murphy for recurrent pleuritic exudates, may be tried with some prospect of success.

When the fluid is serum action will depend upon the duration of the exudate when the patient comes under observation, upon its volume, and upon associated conditions.

Medicinal Treatment.—In the first ten days after the fluid appears medicinal measures are to be preferred unless the exudate is large and causes much dyspnoea or discomfort from pressure. The medicinal measures most generally relied upon are the administration of large doses of salicylate of soda, the giving of Epsom salt in concentrated form, and the use of diuretics.

The salicylate of soda, in doses of ten or twenty grains, in many cases has a decided effect in provoking diuresis and hastening the absorption of pleural exudates. It must be given freely diluted and preferably two hours after food, but even then often causes nausea.

Epsom salt to be effective must be given in as little water as possible, and the amount of water taken by the patient restricted. If a number of watery stools occur there may be some diminution in the pleural fluid. My own experience with the treatment is too small to justify any opinion as to its value.

Of the various diuretics employed the best are infusion of digitalis either alone or with acetate or citrate of potassium; powdered digitalis with caffeine, theobromine sodium salicylate, or benzoate of lithium; or Niemeyer's pill (calomel, squill, and digitalis). Theocin does not appear to have an appreciable effect upon pleural exudates. If under these agents the level of the fluid gradually falls, one is justified in persevering with them.

Autoserotherapy.—In 1894 Gilbert ⁴ read a paper before the Medical Congress at Rome, reporting his results in the treatment of tuberculous pleurisy by injecting into the skin one cubic centimetre of serum withdrawn from the chest. Most of the patients were tuberculous, and a spontaneous pleurisy was assumed to be tuberculous. Of the twenty-one persons treated, in all but two the injection was followed by a reaction with fever. Then the fluid was absorbed gradually and the general condition was improved. All the patients recovered in fifteen days, or at the most three weeks.

Gilbert's method has been tried more recently by several Italians, who are favorably impressed by it, more so than the reports of their cases seem to warrant.

Landolfi ⁵ reports seven cases in most of which the fluid had to be withdrawn by aspiration.

⁴ *Gaz. des Hôpitaux*, Paris, 1894, vol. lxxvii, p. 560.

⁵ *Micheli Landolfi: La Riforma Med.*, 1904, vol. xx, No. 29, p. 818.

Donzello ⁶ reports four cases. He thinks the method promotes absorption and lessens the tendency to its reaccumulation.

Fede ⁷ reports five cases in which he thinks the results were excellent. The urine was increased in most of the cases. A reaction occurred only in one case which was tuberculous. He suggests that as the reaction occurs in tuberculous cases and never in the others the method may serve to differentiate them.

Breathing Exercises.—Rosenthal ⁸ describes a system of pulmonary gymnastics which he has employed with great benefit in serofibrinous pleurisy. He gives the histories of seventeen cases and gives charts showing temperature, pulse, and respiration, the urinary excretion, and the gain in weight. The exercises cause a marked diuresis with increase in excretion of chlorides, and a coincident gain in weight to or beyond the previous maximum of the patient.

During the acute stage, according to the state, the tolerance, and the indications, one may begin with 10 nasal respirations in dorsal decubitus with arms to the side, and progress to a little *séance* comprising 20 nasal respirations in dorsal decubitus with arms to side, 20 diaphragmatic respirations, and 20 respirations with the arm of the sound side put behind the head.

The diaphragmatic respirations are made by inducing the patient to lift in breathing the left hand of the doctor placed without pressure on the abdomen. The following series may also be employed: 20 nasal respirations; 20 diaphragmatic respirations; 10 respirations with flexion of the right limb; 10 with flexion of the left limb. The arm of the affected side is placed across the chest, then lengthwise of the body. Very quickly is reached a series of five exercises repeated 20 times. For example, at the end of the febrile stage, fix the arm by the body, have the patient take 20 nasal respirations, and 20 diaphragmatic, 20 respirations with flexion of the right limb, 20 with flexion of the left limb, 20 respirations with the arm of sound side behind the head. Later comes breathing with both arms behind the head, then with the

⁶G. Donzello: *Gaz. Degli Ospedali*, Nov., 1903, No. 131, p. 1385.

⁷F. Fede: *La Riforma Med.*, 1906, vol. xxii, p. 1319.

⁸Les exercices physiologiques de respiration dans le traitement de la pleurésie sero-fibrineuse (pleuro-tuberculose primitive), Georges Rosenthal, Hayem's clinic, *Archives Gén. de Méd.*, Jan., 1909.

arm of the diseased side behind the head with oscillations or movements of the arm of the sound side. To this unilateral movement succeed unequal oscillations, then progressive oscillations of both arms; finally the bilateral movement is only given very slowly—no active movement. These exercises seem to me to be well worth trying, but my preference would be to try them after aspiration, and not to rely wholly upon them for removal of the fluid.

When the volume of serous exudate is small and causes no embarrassment of breathing, one is justified in waiting and watching. These small exudates occupy a debatable ground as regards treatment. Eventually they may be absorbed under the influence of breathing exercises and measures which improve the general health. When they are not dispensed with by this means they should be aspirated. If, however, the exudate is in volume sufficient to fill the pleural sac, to cause great dyspnoea or cyanosis, or has persisted for weeks in spite of the measures already spoken of, there can be no question but that aspiration should be done at once. Some authors advise against withdrawal of the exudate in the presence of demonstrable disease of the lung, on the ground that the lung kept at rest by the exudate has a better chance of healing. I can see no benefit from allowing the exudate to remain. Doerfler⁹ has noticed that progressing cases of pulmonary tuberculosis seemed to be favorably influenced by an intercurrent pleuritic effusion when the latter was removed by thoracentesis after it had lasted a week. Of forty-five patients only five failed to derive benefit from it. He explains the benefit as due to the hyperæmia which follows removal of the effusion, and compares it to that following laparotomy for tuberculous peritonitis. But as the very occurrence of a pleurisy in tuberculosis of the lung shows a further extension of the disease to a new structure, I should regard any benefit that seemed to follow from it as apparent, not real. We can at least aspirate in those cases of combined tuberculosis of the lung and pleura in which the dyspnoea or oppression is probably due to the pressure of the fluid and not to the lung disease. Almost all men are agreed that when the exudate has remained stationary for any length of time it should be withdrawn. Of course it is not the cause of the pleurisy, neither
+ is pus the cause of an abscess; but its removal is usually a benefit.

⁹ Deutsches Archiv für klin. Med., lxxxiv, Nos. 1-4: Merkel Festschrift (Abst. in Jour. Amer. Med. Assn., Sept. 30, 1905, p. 1036).

Thoracentesis.—In aspirating a chest a trocar and cannula are much safer than a large needle. One of the dangers of the operation is shock, and the shock is probably due to the scratching of the lung by the sharp point of the needle. The cannula should be connected with a bottle in which a partial vacuum has been created. It is not necessary to have a complete vacuum, and it may be dangerous. The fluid in the chest is usually under somewhat increased tension, and will flow out readily without much suction. Where the lung has been compressed for some time it may not be able to expand quickly. If then forced suction is employed, a condition of congestion and œdema of the lung may develop with albuminous expectoration and death.¹⁰

In small effusions the site of thoracentesis must be determined by the seat of the effusion. In large effusions puncture may be made in the seventh or eighth interspace in the posterior axillary line, or in the middle line of the axillary region on a level with the nipple or a little below it. S. West insists that the latter is the preferable place, as the lung is much less likely to be wounded there.

The patient should not be compelled to sit up as though gravity were the sole influence which determined the flow. It is safer to have him lie on his side. Syncope, which sometimes follows paracentesis, may be avoided by posture.

The area around the seat of puncture should be made surgically clean, and the point of puncture made anæsthetic with an ethyl chloride spray. Withdrawal of the fluid may be continued as long as it flows freely; but it should be stopped at once if there is much coughing, or the fluid becomes bloody, or if the heart becomes weak and the blood-pressure falls.¹¹ It is better to make several aspirations at intervals of a few days or a week than to injure the patient by attempting too much at one time. Moreover, a complete withdrawal is not necessary. It is a common experience that after a portion of the exudate is withdrawn nature is herself able to care for the rest. When the fluid reaccumulates the cause is usually tuberculosis or tumor (sarcoma), but not always. These recurrent cases have been successfully treated by opening the chest and

¹⁰ See a case reported by Gerhardt, *Correspondenzblatt für Schw. Aertze*, Basle, May 15, vol. xxxviii, No. 10 (*Abst. Jour. Amer. Med. Assn.*, June 27, 1908).

¹¹ J. A. Capps and D. D. Lewis: *Amer. Jour. Med. Sci.*, Dec., 1908.

introducing a drainage tube, as in empyema. Chapin¹² has reported a non-tuberculous case in which after six aspirations between October 8 and November 14 a cure was effected by injecting one ounce of glycerin containing ten drops of formalin, as suggested by Dr. John B. Murphy. Four weeks after the injection the fluid had disappeared from the chest, and in a month later the patient had gained 10 pounds in weight. Dr. Murphy employs a two per cent. solution of formalin in glycerin, which must be prepared at least twenty-four hours before being used in order to insure complete solution of the formalin. From two drachms to two ounces are used after aspiration of the exudate.

The after-treatment of the patient should cover restoration of function upon the affected side, and treatment for tuberculosis. In cases in which thoracentesis has been done promptly, the lung usually expands very quickly and little thickening of the pleura remains. Deep breathing exercises, such as those already mentioned, or others in which the patient is required to blow water from a full gallon bottle into an empty one, the two being connected by rubber tubes, are very useful in promoting a tardy expansion of a collapsed lung. Tonics are also of great value, the best being quinine, iron, strychnine, and digitalis. Whatever will improve the patient's general health will be a benefit to his pleurisy.

As to the treatment of the cause, the tuberculosis, I have no new word to speak. I constantly urge upon the students to regard every case of pleurisy that occurs without obvious cause as probably tuberculous, and that they should be just as careful in the subsequent management of a case of tuberculous pleurisy as they would be of a patient with incipient consolidation of an apex of a lung. If this were done I am sure there would be many more permanent cures than there are at present. The patient should be kept under observation for several years. The sheet anchors of our treatment are rest, fresh air, hypernutrition. Success depends upon knowing how to obtain these for the patient under the conditions in which he must live, and in inspiring him with hope and courage to continue his long uphill fight until it is crowned with victory. There should be no slavish adherence to even the best diet, milk and eggs. If the patient prefers beefsteak and can pay for it, let him have it.

¹² L. D. Chapin: Boston Med. and Surg. Jour., April 18, 1907, p. 505.

SOME REMARKS ON HYPERCHLORHYDRIA

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UP to a rather recent date most writers, in describing this condition, have considered it as a simple secretory neurosis—a reflex manifestation of a morbid state either in the stomach or elsewhere. In very many cases this is really true, but in some there can be proved a direct and tangible cause for this hypersecretion of hydrochloric acid.

Let us begin by understanding exactly what is meant by the term hyperchlorhydria. There are numerous disorders of the stomach or other abdominal viscera in which hyperchlorhydria is an incident. In gastric ulcer, in duodenal ulcer, and in cholecystitis or cholangitis there is generally an excess of this acid.

The writer some time ago saw a case of persistent hyperchlorhydria where the cause was traced to a stenosis of the small intestine resulting from an adhesive band. Dr. W. P. Nicolson, of Atlanta, personally reported an instance where a patient had been treated persistently for hyperchlorhydria, but where it disappeared immediately after emptying the gall-bladder of a large number of stones. Appendicitis also sometimes lies behind this condition.

Unfortunately many cases of hyperacidity of the stomach contents resulting from an excess of organic acids, and in which there may be absolutely no free HCl, are erroneously diagnosed as hyperchlorhydria. The clinical pictures of these two conditions may present certain common features, and indeed it may be a difficult matter in certain obscure cases to differentiate between them by the symptoms alone.

Again, in deciding the percentage of free HCl by the dimethyl-amido-azo-benzol solution, Toepfer's method, caution should be observed to halt the titration when an *orange-yellow* reaction has been reached, and not carry it on to *lemon-yellow*. Failure to observe this will place an unfairly large number in the hyperchlorhydric class.

It is also necessary to distinguish between hyperchlorhydria and hypersecretion, though it is possible for both to be present at the same time, and in the latter hyperchlorhydria may be found at the height of digestion.

Now, while this trouble may begin as a secretory neurosis from causes to be mentioned, Einhorn, Hemmeter, Reed, and Cohnheim agree that later on there will be proliferation of the glandular elements of the stomach. It is rare that the opportunity to examine these stomachs presents itself; but Hemmeter reports four in which death occurred from an intercurrent disease, and the writer wishes to report one. In all of these glandular proliferation was found with increase of oxyntic cells in the intermediate zone and fundus. Let us then consider this perversion of gastric secretion to be a neurosis only when we can demonstrate by exclusion the absence of either indirect or organic causes.

Etiology.—It is not agreed as to the fundamental causes of hyperchlorhydria. We can safely enumerate, however, many of the predisposing factors, and in that way throw some light upon the effects which stand out most prominently.

Hyperchlorhydria is encountered more frequently in cities than in the rural districts. Excitable people, or those with unstable nervous systems, are prone to suffer from the affection more often than persons of phlegmatic disposition. Jolly noted it often in hysterical patients, while Von Noorden met with it in neurasthenics and melancholics. Strange to say, it is more frequent in men than in women. The refined, the educated classes, and those whose labors require mental tension are the most frequent sufferers, though Hemmeter mentions it as not infrequent among manual laborers. The writer's experience has been entirely different from that of Hemmeter, for only in the rarest instances has he found this neurosis in those who earned their bread by physical toil. In the rush and hurry of life to which our American civilization is becoming more committed with each passing year, we may expect to see this perversion of the function of the gastric secretion increase steadily.

Age, too, is an important factor, youth and middle life furnishing the majority of cases.

Riegel considers chlorosis an etiological factor worth noting.

Oswald reports on twenty-one cases of chlorosis, twenty of which showed a marked excess of HCl in the gastric secretion. In this conclusion the writer agrees.

Psychic influences of various sorts seem to set in motion this morbid train of symptoms. Fear, worry, hate, sorrow, or mental perturbation of any kind may cause it. The writer recently examined test meals from twelve ordinarily healthy young medical students who were "cramming for a final." In every one the HCl was considerably above the normal mark.

Sometimes it would appear that the hyperchlorhydria originates from some abnormal irritation of the gastric mucosa kept up for a long period of time. Among such causes may be cited poor mastication, hasty eating, drinking large quantities of ice-water or hot drinks, spices or sharp condiments, or alcoholic excesses. Any of these may set up a certain amount of gastritis, which, on disappearing, may leave in its wake irritable and hypersecreting oxyntic cells.

Hyperchlorhydria is generally present when there is ulcer of the stomach, but whether in the rôle of cause or effect is a question *sub judice*. The writer does not feel safe in asserting more than the following: If hyperchlorhydria is present with an ulcer, conditions are much less favorable for healing of the ulcer; while we feel sure that over-secreting stomachs furnish a much more ready surface for the development of ulcerative processes.

Dr. Boardman Reed considers that in a certain proportion of the worst cases of hyperchlorhydria there is probably a latent ulcer as the etiological factor. In still other cases Reed believes that the rough scars of healed ulcers act as constant irritants. He has come to this conclusion from a study of cases in which there had been undoubted gastric or duodenal ulcer, and in which there continued an excessive secretion of HCl for from six months to a year after all signs of existing ulcer had disappeared. Let us not forget that eye-strain may furnish its share of offense. In female patients any pelvic troubles should be investigated, and movable kidneys should not be overlooked.

Men who smoke too much will frequently be found to be suffering from hyperchlorhydria, though a careful examination will generally disclose the fact that an acid gastritis is also present.

Symptomatology.—The symptoms of hyperchlorhydria vary greatly. Riegel asserts that in a not infrequent number no symptoms may be complained of, but in every case the writer has ever observed the patient was aware that something was wrong with the digestion. The symptoms always develop after eating, the nature of the discomfort depending much on the variety of food which is taken.

Let us sketch the picture most often presented: The patients are fairly well nourished, have a good appetite, complain of some frontal headache, are generally constipated, and give a history of more or less mental depression.

In from half an hour to three hours after eating there comes a pain in the region of the stomach, burning, boring, or gnawing, and radiating towards the back. This pain is not relieved by change in position, but is often ameliorated by eating more, or drinking water or milk. There is also formation of gas, burning eructations, perhaps nausea, followed by vomiting very acid quantities of partly digested food. If, during the belching, small amounts of the acid contents are brought up frequently, it exerts a caustic action on the œsophagus, giving rise to heart-burn, or a severe contracting pain under the sternum extending to the pharynx. This is called by Sticker “pyrosis hydrochlorica.”

Ordinarily one would expect an increase of the motor function on account of the increased irritation; but in many instances the opposite condition obtains, brought about by cramp of the pylorus. This may lead later on to fatigue of the pyloric musculature, atony, and dilatation of the stomach.

After the stomach is emptied, or after vomiting, the patients quickly feel relieved and seem perfectly well. In some the symptoms appear only after certain kinds of food are ingested, and many of the patients have learned by experience what to avoid.

There is rarely any pain at night, this being a symptom pointing to hyper- or continuous secretion.

The external examination seldom discloses anything abnormal. Between the attacks the region of the stomach, as a rule, is not tender on pressure; but during the pain there is generally some tenderness with occasional hyperæsthesia. This differs from ulcer in that the tenderness is diffused over a considerable area.

There may be many deviations from the foregoing description, and even in a classical grouping of all these symptoms, a diagnosis cannot be made with certainty until the stomach contents after one or more test meals are intelligently examined.

In hyperchlorhydria the free HCl often reaches as high as 80 or 100, while the total acidity may reach even 150. Organic acids have nothing to do with hyperchlorhydria proper; neither does gaseous fermentation, which generally indicates dilatation or motor insufficiency. There is no excess of stomach mucus as is found in the different grades of gastritis, and, should much be present, the diagnosis of hyperchlorhydria as a pure neurosis may be eliminated.

The digestive power is fairly good, and, if there is not too much starchy food eaten with the proteids, the former will leave the stomach at the same time, unless marked motor insufficiency is present.

Absorption is also good, as may be proved by the iodide of potassium test.

Other symptoms vary greatly with the individual, while the excess of acidity fluctuates within wide boundaries. All the symptoms may be absent for weeks, only to be brought on again by a variety of causes either material or psychic.

Diagnosis.—This is reached by careful examination of stomach contents, and exclusion, as far as possible, of the other exciting factors mentioned. Patience and tact will be needed, and even then the physician should not be too positive until several tests under varying circumstances have been made.

Prognosis.—In uncomplicated hyperchlorhydria, the prognosis is favorable. A patient and careful observance of proper methods of treatment will almost invariably afford relief. Where there are complications the prognosis, of course, will be governed according to their importance and severity.

Treatment.—Bearing in mind that hyperchlorhydria is either a neurosis, or the manifestation of some morbid process lying behind the hyperchlorhydria, we should diligently seek to remove, as far as practicable, disturbing conditions. A search should be made for the abnormal reflexes, for they can often be abated.

With kindly sympathy endeavor to lift the veil that may be

hiding worry, grief, financial stress, or carping care. No glands in the whole human body are more susceptible to the ebb and flow in the tides of emotion than those of the stomach. It may not always be feasible to remove these disturbing mental factors, but attention may at least be drawn to their importance, so that intelligent efforts may be centred in that direction. Just along this line the various cults of mental healing, religious and otherwise, have won some of their spectacular victories.

If the gall-bladder or bile-ducts are responsible, they must be treated medically or attacked surgically as may be indicated. Where stenosis, due to narrowing of the bowel or pressure from bands or adhesions, is present, or where a chronic appendicular inflammation is exerting a malign influence, operative measures alone will afford relief.

Gastritis, acute or chronic, gastric or duodenal ulcer, or any irritant which keeps the oxyntic cells unduly stimulated must be cured before we can hope to reduce the acid excess.

The diet should of course be bland. Sodium chloride should be restricted; while spices, condiments, rich sauces, and acid fruits or acid soft drinks should be forbidden. When we come to the consideration of proteids we find ourselves between Scylla and Charybdis, for, while proteids are theoretically indicated to combine with the HCl, they also tend to increase its secretion. Frequent meals would also be theoretically indicated to keep the acid juice at work on the food, instead of permitting it to irritate the mucosa. It is best, therefore, to allow some red meat, excluding viscera and soup extractives, giving liberally milk, eggs, custard, and cereals on account of their proteid content; also fat meat, cream, starchy vegetables such as potatoes or sweet potatoes, and plenty of sugar or syrup. Enjoin thorough mastication, and the avoidance of all irritants in food, such as seeds, peelings, or woody fibres. Tea and coffee should be prohibited; but cocoa, being an excellent HCl binder, may be allowed with milk and sugar. A German preparation called Hemo-Cocoa, containing hæmoglobin, recently introduced in this country, has been found by the writer to be a satisfactory beverage where some anæmia was present.

Cold, or even ice-water may be given when the pain indicates high acidity, but alcoholic or carbonated drinks are never helpful.

It is well to allow hearty meals which should not be taken too often, for a small meal stimulates the flow of gastric juice as much as a large one, but fails to bind much of the acid.

Some advise the taking of more food when the pain becomes severe; but it may be considered a bad practice to superimpose one meal upon another not fully removed from the stomach, and the acidity may be preferably counteracted in other ways.

Extract of belladonna an hour to half an hour before meals will exert a marked influence in reducing the amount of secretion. The writer uses it in doses of $\frac{1}{8}$ to $\frac{1}{10}$ gr., though Dr. Wm. Van V. Hayes, of New York, uses $\frac{1}{50}$ gr., and Dr. Theodorus Bailey $\frac{1}{25}$ gr., with satisfactory effect.

Where the gastric mucosa is unduly sensitive, this combination will exert a sedative effect, if given half an hour before meals: Tr. belladonna 2 minims, sodium bromide 5 gr., chloral hydrate 1 gr., and chloroform water enough to make 1 drachm, in each dose.

After the meals different alkalies in various combinations should be ordered, but the time for their dosage should be governed by the individual symptoms. Nutrition being interfered with if alkalies are taken too soon after eating, it is better to give rather a small dose as late as the pain will permit, even if it becomes necessary to repeat it one or more times, as the excess acid manifests itself.

Combinations of calcined magnesia, bismuth, or sodium bicarbonate, to which may be added rhubarb if a more laxative effect is required, may be administered in varying proportions, and directed in half to one drachm doses, beginning from half an hour to two hours after meals. Should the powder be objectionable to the patient, milk of magnesia may be substituted, and to this may be added other ingredients as indicated.

As to local treatment there is some discussion, but in view of the fact, which is now generally accepted, that the gastric mucosa in hyperchlorhydria is exceedingly sensitive, the writer feels justified in commending lavage, first with plain water, then with silver nitrate 1:2000, then with plain water again. This has yielded gratifying results in several instances recently under observation. It will readily be seen how beneficial this lavage would be, should there be present a latent ulcer.

Intragastric treatment with the high tension coil will aid those

cases where there is deficient motor power in the gastric muscle, but otherwise its effects can only be psychic, and its use will often be disappointing.

The foregoing remarks fairly cover the field regarding this disease up to the present date, but the last word has by no means been spoken; and it may be confidently predicted that, from the labors of many careful students now focusing their efforts towards the control of this painful affection, we may reap an early and profitable harvest.

CONGENITAL FAMILIAL SPLENOMEGALY WITH CHRONIC ACHOLURIC JAUNDICE

ALSO A CONSIDERATION OF THE VARIOUS TYPES OF JAUNDICE
ASSOCIATED WITH SPLENIC ENLARGEMENT IN EARLY LIFE

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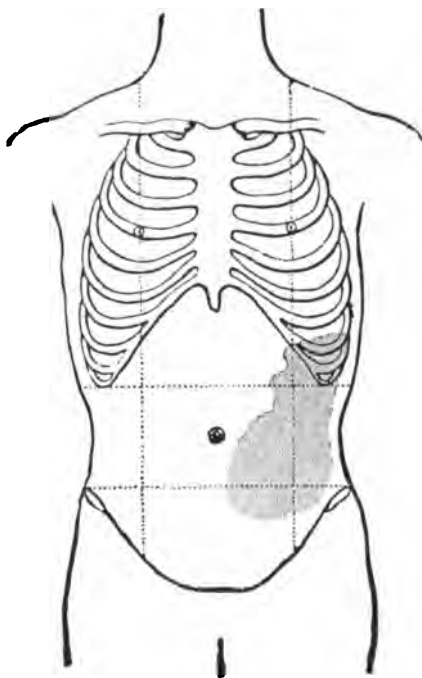
THE patient, Ernest N.,¹ is a fairly well developed boy, aged 14 years, but he looks somewhat anæmic, and his conjunctivæ have a slight but distinct icteric tinge. The spleen (see Fig. 1) is evenly enlarged and hard, reaching downwards to the anterior superior iliac spine. The liver cannot be felt and is apparently not enlarged; the fæces are not acholic. The urine is generally of rather low specific gravity, clear, pale, and free from albumin, sugar, and bile-pigment, but it sometimes shows excess of urobilin. The blood-serum was kindly examined by Mr. L. S. Dudgeon, in November, 1908, at a time when clinically the jaundice was scarcely recognizable, and was found to contain bile-pigment. The thoracic organs and other parts of the body do not show anything abnormal, excepting that on one occasion a systolic murmur was heard over the mid-cardiac area, probably not due to organic disease. The fingers are not clubbed; no enlargement of superficial lymphatic glands or tonsils is present; there is no pruritus or cutaneous affection.

The blood, examined during the periods in which the boy was nearest normal, sometimes shows the presence of a few normoblasts; of two rather large-sized normoblasts seen in a blood-film of January 21, 1909, one had a double nucleus. In another blood-film of the same date several normoblasts and one myelocyte were found. The red cells vary much in size ("anisocytosis") and staining ("polychromatophilia"). The average diameter of the red cells does not appear to be increased, as it often is in chronic obstructive

¹ The patient was shown at the Clinical Section of the Royal Society of Medicine in London on February 12, 1909.

jaundice, but if anything it is rather below the normal standard. A blood-count on November 6, 1908, gave 2,800,000 red cells, and 14,280 white cells to the cubic millimetre; the differential count of white cells (kindly furnished by Dr. A. E. Boycott) gave lymphocytes 20.6 per cent.; intermediates 4.8 per cent.; large hyalines 4.4 per cent.; neutrophile polymorphonuclears 68.4 per cent.; eosinophiles 1.0 per cent.; mast-cells 0.8 per cent. (no nucleated red cells seen

FIG. 1.



Showing size of the spleen on January 21, 1909, in the patient Ernest N.

on that occasion). A blood-count of a later date (January 21, 1909), gave 3,140,000 red cells and 14,500 white cells; hæmoglobin, 70 per cent. Examination of blood-films, as already stated, showed the presence of a few nucleated red cells. Dr. A. E. Boycott, who kindly looked over stained blood-films of that date, reported that there was a tremendous amount of variation in size and depth of staining amongst the red cells; most of the red cells were a good deal too small, but on the other hand, there was no poikilocytosis

to speak of.* There was much "anisocytosis" with very little poikilocytosis. The resistance of the red cells toward hæmolysis has been tested on various occasions by Ribierre's method²; it is found that hæmolysis occurs when a few drops of the patient's blood, diluted with normal saline solution, are added to a solution of between 0.40 and 0.48 parts per cent. of sodium chloride in distilled water (the resistance to hæmolysis was greatest on January 21, 1909). There does not, therefore, appear to be very decisive evidence that the chronic acholuric jaundice is "hæmolytic" in the present case; at all events, the evidence that it is due to congenital fragility of red cells is insufficient, though the fragility of the patient's red cells towards distilled water does really appear to be slightly greater than the average in normal individuals who were used as controls. In this connection an observation kindly made with the boy's blood by Mr. L. S. Dudgeon on November 25, 1908, is also interesting. Mr. Dudgeon found that the patient's blood-serum did not exert any hæmolytic action on the red corpuscles of a healthy individual, or on the red corpuscles of the patient himself (that is to say, it had no autohæmolytic action); nor had blood-serum from a normal individual any hæmolytic action on the patient's red cells.³

The history is that the patient was born at full term with the help of instruments, and was very yellow at birth. The jaundice never completely disappeared; his eyes (sclerotics) have always presented a slight yellowish tinge, but his complexion has generally

* From the blood-films taken from the boy Ernest N. on January 21, 1909, Dr. A. E. Boycott afterwards made the following differential count of 500 white cells: lymphocytes 20.4 per cent.; intermediates 5.6 per cent.; large hyalines 3.2 per cent.; neutrophile polymorphonuclears 66.8 per cent.; eosinophiles 3.2 per cent.; mast-cells 0.8 per cent. Whilst counting the 500 white cells he found 20 nucleated red cells: four of these were typical normoblasts; two were normoblasts with budding nuclei; and 14 were nucleated red cells of the ordinary type with polychrome cytoplasm, irregular in shape and about the size of a typical normoblast. There was much polychromatophilia present. The red cells showed marked variation in size (mostly on the small side), but hardly any poikilocytosis.

² I have to thank Dr. Chapuis, one of the house physicians at the German Hospital, for much assistance in the examination of the case, particularly in regard to the question of hæmolysis.

³ For Mr. Dudgeon's methods in this respect see his recent paper on the subject in the Proc. Roy. Soc., London, 1908, series B, vol. lxxx, p. 531.

been sallow rather than distinctly yellow. He has been always subject, however, to recurrent attacks of "depression," during which his urine becomes darker and he appears yellower and suffers from lassitude and drowsiness. These attacks recur about every three months on the average and last a few days. Recently he suffered occasionally from severe abdominal pains of uncertain character. Occasionally on blowing his nose he has noticed spots of blood on his handkerchief; but he has never had a regular attack of epistaxis and has never had bleeding from the gums or any other form of hemorrhage, excepting a mild attack of purpura in 1899, when he was four or five years old. At that time, according to Dr. Porter Parkinson's account (see later), the blood contained many small nucleated red cells (microblasts). His spleen was apparently first noticed to be large when he was three months old. He has always been subject to nocturnal enuresis. He has had no other illnesses except "croup" at one year of age.

There is no probability of a congenital syphilitic taint. The patient's father and mother both look healthy. The mother, now aged 48, has had thirteen children and no miscarriages. The eldest four children died early; the fifth, sixth, and seventh are living and healthy; the eighth is the present patient; the ninth, tenth, and thirteenth are living and healthy; the eleventh died as a baby; the twelfth, a girl with anæmia and splenomegaly without any jaundice, died at the age of one year and eight months. Both she and the present patient were shown in 1905, by Dr. Porter Parkinson, at the Society for the Study of Diseases in Children.⁴ Though there was no distinct jaundice in this girl Dr. Parkinson stated that the skin had a lemon-yellow color. Doubtless her blood would have been found to contain bile-pigment just as that of her brother does at present. Her spleen reached down to the anterior superior iliac spine and the liver could be felt one finger's breadth below the costal margin. Her red blood-corpuscles varied much in size (none very large) and numbered 3,393,000 to the cubic millimetre of blood. Her white corpuscles numbered 52,570, and the differential count gave polymorphonuclears 42 per cent., eosinophiles 10 per cent., small mononuclears 36 per cent., large mononuclears 9 per cent., and myelocytes 3 per cent. A most interesting point is that the

⁴ See the Society's Reports, London, 1906, vol. vi, p. 8.

mother says that all her children were born yellow and remained yellow for three to six months after birth, but the jaundice was permanent in the present patient only.

Before proceeding further I would state at once that the icterus neonatorum in these children was probably merely an exaggerated form of the so-called "physiological icterus neonatorum." The cause of "physiological" jaundice in new-born children is still uncertain; but whatever it may be, it seems to affect some families more than others. There have been families in which some of the children were affected with a harmless though prolonged form of icterus neonatorum, whilst others have succumbed to a fatal disease termed "icterus gravis neonatorum," which, according to Pfannenstiel,⁵ is certainly not septic in origin, but is merely an extremely severe form of the so-called "physiological icterus neonatorum"; in icterus gravis neonatorum, as in the physiological icterus neonatorum, the faeces are not acholic; and the results of post-mortem examination tend to show that the disease is to be distinguished from congenital obliteration of bile-ducts, with which it has probably sometimes been confused.

In order to illustrate the probable nosological position of the present case (Ernest N.) I shall now consider the main features of the various classes of cases characterized by chronic jaundice and enlargement of the spleen or of the liver, or of both of these organs, in early life. With few exceptions all such cases may be classified under one of the four following heads: (1) Congenital obliteration of bile-ducts and obstructive jaundice, probably connected with a congenital form of cholangitis; (2) inherited syphilis; (3) biliary cirrhosis; (4) chronic acholuric jaundice with enlargement of the spleen or of both the spleen and liver.

The occasional occurrence of very exceptional cases not coming under one of these heads can be easily imagined. For instance, hydatid cyst of the liver, causing enlargement of the liver, in a child may give rise to obstructive jaundice by pressure on the bile-ducts, or may be associated with a toxæmic catarrhal jaundice and splenomegaly. In the case of a boy shown by Dr. A. F. Voelcker at the Medical Society of London in November, 1907, there was en-

⁵ See J. Pfannenstiel: "Über den habituellen Icterus gravis der Neugeborenen," Muenchener med. Wochenschrift, 1908, vol. lv, p. 2169 and p. 2233.

largement of the liver and of the spleen, together with a past history of jaundice (in 1902), which was recovered from. The hepatic enlargement was due to a hydatid cyst, which was afterwards successfully treated by operation; but a certain amount of splenomegaly remained in February, 1909, when Dr. Voelcker showed the boy again at the same Society.

1. *Congenital Obliteration of Bile-ducts and Obstructive Jaundice, Probably Connected with a Congenital Form of Cholangitis.*

In the cases generally termed "congenital obliteration of the bile-ducts," such as those so carefully collected and discussed by John Thomson⁶ in 1892, the jaundice is sometimes present at birth, but it may not be noticed till the second or third day, or may occasionally appear a few days later. It rapidly becomes intense and is distinctly obstructive in character. The urine is bilious. After the meconium, which is sometimes apparently normal, has been passed, the fæces are nearly always acholic,⁷ but as a rare exception they may be (*e.g.*, after a dose of mercury) slightly colored. The liver and spleen are both generally enlarged. Death always occurs within eight months. The lesions found in the liver and bile-ducts seem to be the result of a chronic cholangitis, but in some cases no actual obliteration of bile-ducts has been found. The exact site of the obliteration, when present, varies in different cases. Thomson⁸ says: "The inflammatory lesions follow the course of the bile so closely that we can scarcely avoid the conclusion that they are secondary to some irritating change in the character of this fluid. That inspissated bile and gall-stones should have been found is, therefore, of importance. The frequent occurrence of complete stoppage of the passage of bile before there is any absolute anatomical blocking of the lumen of the ducts is also worthy of note, and suggests the possibility of a descending catarrh from irritating bile, such as is said to occur from poisoning by toluylendiamine and other substances (Stadelmann, W. Hunter)." Rolleston and

⁶ J. Thomson: "On Congenital Obliteration of the Bile-ducts," Edinburgh, 1892.

⁷ In regard to fæces the epithet "acholic" is used to signify not merely that they are without bile-pigment, but likewise that they do not contain coloring matter derived from bile-pigment.

⁸ J. Thomson: Allbutt's System of Medicine, 1897, vol. iv, p. 256.

Hayne,⁹ in recording a case of the disease in a child who lived six months, suggested that the disease was primarily started by poisons derived from the mother and conveyed to the liver of the foetus, and that a mixed cholangitis and cirrhosis was thus set up. This cholangitis, starting in the smaller biliary channels and descending to the larger bile-ducts, might lead, they thought, to the inflammatory obliteration of extrahepatic ducts.

If these views be correct one can easily understand that abortive forms of the disease may occasionally occur from which recovery is possible. Thomson points out that "a few cases of infantile jaundice have been reported as ending in recovery which, from their symptoms, and from their occurring in the same families as other children with obliterated bile-ducts, seem possibly to have been cases of this disease (Anderson, Freund, Grandidier)." At a meeting of the Society for the Study of Diseases in Children on February 16, 1906, F. J. Poynton¹⁰ described two interesting cases of chronic obstructive jaundice in infants aged three months and one month respectively. In his first case the jaundice was present at birth; in the second it appeared on the third day. The liver in both cases was large and not tender. The spleen could not be felt. The stools were generally acholic, large, and fatty, but in both cases occasionally slightly colored. In both cases recovery ultimately took place. Poynton attributed the condition to excessive viscosity of the bile and possibly also unusual smallness of the biliary channels. It seems to me that (allowing Dr. Poynton's explanation to be correct) the viscid condition of the bile and narrowing of bile-channels in cases like those he described might result from a minor form of descending cholangitis of the same type as that which in more advanced degree might produce the characteristic symptoms and fatal progress of so-called "congenital obliteration of the bile-ducts."

It is quite possible that the following case now under my care at the German Hospital belongs to the same class. The patient, Willie W., when aged three months, was admitted (January 25,

* Rolleston and Hayne: "A Case of Congenital Hepatic Cirrhosis with Obliterative Cholangitis," *Brit. Med. Journ.*, 1901, vol. i, p. 758.

* Poynton: *Reports of the Society for the Study of Diseases in Children*, London, 1906, vol. vi, p. 173.

1909) suffering from malnutrition and jaundice of moderate degree. According to the mother the child had been jaundiced from birth. Both the mother and the father were said to be healthy. They had had only two other children, who were both living and healthy. There was no other history of jaundice in the family. The mother had had no miscarriages. In the hospital the child's liver was found to be enlarged but not tender to palpation. The spleen could not at first be felt. The fæces were acholic and rather copious. The urine was free from albumin and sugar, but gave a positive Gmelin's reaction for bile-pigment; one or two granular casts were found. The heart and lungs showed nothing abnormal. There was no enlargement of superficial lymphatic glands. No cutaneous, retinal, or other hemorrhages were noted. Blood-examination (January 30, 1909): Hæmoglobin (by Haldane's method) 90 per cent.; red cells 3,900,000 in the cubic millimetre; white cells 9375; the differential count of white cells (kindly made by Dr. J. C. G. Ledingham) gave small lymphocytes 1.4 per cent., large lymphocytes 25.6 per cent., large mononuclears and transitionals 8.4 per cent., neutrophile polymorphonuclears 61.0 per cent., eosinophiles 3.5 per cent., mast-cells 0.1; no nucleated red cells were seen. The average diameter of the red cells seemed to me distinctly above the normal (it was probably above ten micromillimetres, and this would correspond to the high color-index noted (nearly 1.2), and, according to French observers, might be connected with the obstructive jaundice. Moreover, the resistance of the red cells towards hæmolysis, as estimated by Ribierre's method, appeared rather above the normal standard; this again French authorities have maintained to be the general rule in cases of obstructive jaundice. Thus, on January 30, hæmolysis occurred (Ribierre's method) when a few drops of the patient's blood, diluted with normal saline solution, were added to a solution of between 0.34 and 0.36 part per cent. of sodium chloride in distilled water. After admission the child at first lost weight, but has lately gained weight, and looks less shrivelled and much happier. On January 25 the weight was 8 lbs., 8 oz.; on February 1 it was 8 lbs.; and on February 22 it was 9 lbs., 7 oz. The jaundice has very decidedly diminished, though it varies in degree from time to time. The stools are still practically acholic and the urine contains bile; but quite recently, the early part

of March, 1909, a very slight yellow coloration has been observed on several occasions in the faeces. The liver is decidedly enlarged, but not tender, and not much if at all of harder consistence than normal; in the right nipple line it extends downwards nearly to the umbilical level. The spleen seems to have increased in size since admission, for its lower border can be distinctly felt about one inch below the costal margin. The improvement in the child's general condition is, on the whole, so decided that the case may perhaps be one of mild congenital cholangitis with blocking of bile-channels by viscid mucus. Slight fever (up to 100°F.) was noted on four evenings during the first fortnight in the hospital, but lately the temperature has generally been subnormal, and has only once reached 100° F. A little sodium bicarbonate is being given in the hope of rendering the bile less viscid. Asses' milk (recommended by Dr. Poynton¹¹) is difficult to obtain for hospital cases in London.

2. *Inherited Syphilis*.—In the diffuse pericellular (intercellular) cirrhosis of intra-uterine and early postnatal life (a condition which is generally first recognized at post-mortem examination) jaundice may be present. The whole liver is infiltrated with small cells and the local presence of the *Spirochæta pallida* can be demonstrated by proper methods of staining.¹² In older children splenomegaly occurs as a late manifestation of inherited syphilis and is sometimes associated with enlargement of the liver and occasionally with jaundice. The diagnosis may be very difficult, but is sometimes facilitated by signs of syphilis in the bones (*e.g.*, nodes on the tibiæ, by the presence of Hutchinsonian teeth or other "stigmata" of inherited syphilis, by the past history of the case, or by the family history and by the presence of manifestations of inherited syphilis in other children of the same parents; sometimes the diagnosis is only cleared up by the results of antisyphilitic treatment. If Wassermann's serum-reaction for syphilis were found

¹¹ Poynton: *loc. cit.*

¹² The *Spirochæta pallida* was demonstrated in the liver of infants with inherited syphilis soon after the discovery of the organism in question by Schaudinn and Hoffman in 1905. Amongst the more recent papers on the subject see especially "The Occurrence and Distribution of the *Spirochæta pallida* in Congenital Syphilis," by James McIntosh, *Journ. of Path. and Bact.*, Cambridge, 1909, vol. xiii, pp. 239-247.

to give reliable results it would be of great diagnostic use in these cases. Dr. Robert Hutchison¹³ thinks that in children with splenomegaly as a late manifestation of inherited syphilis the splenic disease is sometimes accompanied by a gummatous enlargement or syphilitic cirrhosis of the liver. As a possible example of such an association and as illustrating the difficulty in diagnosis in the absence of undoubted signs of inherited syphilis, I will give the following short account of a case now under my care, though at the present moment the enlargement of the spleen and liver is not accompanied by jaundice.

The patient, J. B.,¹⁴ a boy aged 11 years, was admitted to the German Hospital in December, 1908, with chronic enlargement of the liver and spleen, and having a rather cachectic appearance, though not really anæmic. The liver bulged forwards in the epigastric region and its lower edge could be felt two finger-breadths below the costal margin in the right nipple line. The spleen was easily felt; it was of rather hard consistence, and reached two or three finger-breadths below the ribs. The thoracic organs showed nothing abnormal, except slight impairment of resonance at the apex of the left lung. Skiagrams (Dr. Finzi) of the lungs gave no evidence of disease at either apex. There was slight nasal obstruction, apparently due to chronic nasal catarrh and some dried blood in the nasal fossæ. No adenoid vegetations (Mr. G. F. Jenkins) or hypertrophy of tonsils were found. A few small lymphatic glands could be felt in the neck, but otherwise there was no enlargement of the superficial glands. The teeth were not well-formed, but were not distinctly "Hutchinsonian." There was a decided tendency to frequent slight bleeding from the lips or gums and from the nose (not regular epistaxis). There were a few hair-like telangiectases on the face and a small "spider-telangiectasis" on the chin. There was no jaundice and no œdema. Ophthalmoscopic examination showed nothing abnormal in the fundi (Dr. C. Markus). There was no fever. The bowels were regular. Urine:

¹³ See his remarks on splenomegaly as a late manifestation of inherited syphilis in the Discussion on Non-leukæmic Enlargements of the Spleen at the Annual Meeting of the British Medical Association, 1908 (British Medical Journal, 1908, vol. ii, p. 1156).

¹⁴ This patient was shown by me at the Medical Society of London February 8, 1909. .

specific gravity 1016; acid; free from albumin and sugar. Examination of the blood (December 15, 1908) showed: red cells 6,000,000, and white cells 7000 in the cubic millimetre; hæmoglobin (by Haldane's method) 100 per cent. A differential count of 500 white cells (kindly made by Dr. A. E. Boycott) gave: lymphocytes 47.4 per cent.; intermediates 7.0 per cent.; large hyalines 4.0 per cent.; neutrophile polymorphonuclears 37.2 per cent.; eosinophiles 1.4 per cent.; mast-cells 3.0 per cent. No nucleated red cells were seen; the red cells seemed normal. Examination of the blood by Ribierre's method showed that there was no diminished resistance of the red cells to hæmolysis. Calmette's ophthalmoreaction for tuberculosis and Von Pirquet's cutireaction both gave a negative result.

In the hospital under treatment by a medicine containing iodide of iron and iodide of potassium the boy's general health has decidedly improved; he has put on flesh and has become more cheerful-looking; his liver has somewhat diminished in size and his spleen though still moderately enlarged does not feel hard. On different occasions the number of red cells in his blood has been found to vary between 5,500,000 and 7,000,000 to the cubic millimetre. This slight degree of polycythæmia may be in whole or part secondary to nasal obstruction, but it may likewise be in some way connected with circulatory obstruction from abdominal visceral disease.

According to the patient's mother the boy had pneumonia and pleurisy in the summer of 1907, and again in the summer of 1908. In 1907 his eyes had a yellowish color, she thinks. For a year or so his abdomen has been rather prominent. There is no history of a rash or skin-eruption during infancy, but he had rather a tendency to snuffles. The mother thinks she herself has always been healthy. She has been married twice. By her first husband she had three children, who are still living and healthy; none born dead; no miscarriages. By her present husband (said to be healthy) her first two children (seen by Dr. Weber) are apparently healthy; the third one is the present patient. Since his birth she has had one child born dead, and one miscarriage.

3. *Biliary Cirrhosis (Hanot's Disease).*—There is a form of hepatic cirrhosis, accompanied by jaundice and (usually great) enlargement of the spleen, which may be termed "biliary" cir-

rhosis, though in the livers from such cases when they finally come to be examined at necropsies the cirrhotic process is seldom or never strictly unilobular, excepting at spots here and there. The disease is mainly one of childhood and the period of growth, but may commence in later years (as in Hanot's original cases). The usual features are: Jaundice, which is generally deep, but varies from time to time, increasing with exacerbations of the disease; enlargement and hardness of the liver; enlargement (often extreme) of the spleen. There is generally a great tendency to bleeding from the nose, gums, etc. The *faeces* are generally not completely acholic, though the urine is rich in bile-pigment. Ascites, when it occurs, is usually a terminal phenomenon. When the disease commences early in life it leads to stunting of the child's growth by partial arrest of development or infantilism. In some cases "clubbing" of the fingers has been observed. This type of cirrhosis, like some other forms of jaundice and hepatic disease, occasionally occurs in two or more members of the same family.

In regard to the size of the liver, though the organ is always enlarged in the typical cases, there seems to be no doubt that it may shrink, as in other forms of cirrhosis, provided that the patient lives long enough. This is, I believe, what took place in the following case:¹⁵

The patient, a girl, J. S., aged 14 years, was under my care at the German Hospital, where she died in February, 1895. She had, her father thought, been more or less jaundiced all her life, and had always been weakly and thin, though she had never had any serious acute illness. She had, I think, repeatedly had bleeding from the nose and gums. She was extremely ill-developed for her age, and looked very much younger than she really was. Her skin was jaundiced and likewise much darkened from chronic pigmentation; there were two or three capillary "stigmata" ("spider-telangiectases"). The liver could be felt considerably below the costal margin, but the spleen was excessively large, reaching a point below the anterior superior iliac spine. There was irregular fever

¹⁵ See F. P. Weber: "Simple Persistent and Congenital Persistent Jaundice, Family Biliary Cirrhosis, and Family Tendency to Jaundice," *Edinburgh Medical Journal*, August, 1903, pp. 111-120. This paper contains many references to French and other literature on biliary cirrhosis in children.

and, during the last weeks, ascites. One sister was said to have become jaundiced at about the age of thirteen years and to have died at nineteen years with symptoms somewhat resembling those of J. S. At the necropsy on the latter the liver was green, hard, and "hobnailed." Perhaps I ought to have described it as having an irregular, scarcely amounting to hobnailed, surface. It only weighed $26\frac{1}{2}$ ounces. Microscopic examination of the sections showed a large amount of fibrous cicatricial tissue, dividing the glandular substance into unequal compartments and sometimes invading the lobules, entering between the individual hepatic cells. There was a good deal of small-cell infiltration in the scar-tissue, showing the progressive nature of the disease. There was no very great increase of bile-canaliculi, but much green inspissated bile could be seen situated between or in the hepatic cells, which, on the whole, appeared to contain relatively little fat. The gall-bladder contained a moderate amount of clear, almost colorless, fluid. The common bile-duct was unfortunately not examined. There was no perihepatitis. The spleen, uniformly enlarged, weighed $20\frac{1}{2}$ ounces; on section its substance seemed rather firm, but otherwise normal; the microscope showed increase in fibrous tissue, and considerable deposit of pigment in some of the trabeculæ. The lymph-glands, especially those at the hilum of the liver, were somewhat enlarged and much pigmented.

In the case (J. S.) the long duration of the disease and its early (possibly congenital or even antenatal) commencement are specially to be noted. Hence the growth and development of the whole body were impaired or partially arrested. The "hypertrophic" cirrhosis had time to become to some extent "atrophic" owing to the gradual contraction of scar-tissue. Doubtless the nodules which gave the surface of the liver an almost "hobnailed" appearance represented a compensatory attempt at regeneration of the glandular tissue of the organ.

In regard to the pathology of biliary cirrhosis I am in favor of regarding the disease as due to an "excretory" irritation of the hepatic glandular cells and minute bile-ducts resulting from the excretion by the hepatic cells of some toxic material or materials of unknown origin and unknown nature. H. D. Rolleston suggested that the "excretory" irritation in question might be due to

a poison arriving by the blood, as in experimental poisoning with toluylendiamine and other substances in animals (Stadelmann, W. Hunter). This theory amply accounts for the main difference between ordinary cirrhosis and cirrhosis of Hanot's type. In the latter form of cirrhosis large numbers of the minute bile-capillaries probably become blocked with plugs of inspissated mucus, so that, although bile from many hepatic lobules can usually still reach the intestine and for long periods prevent the faeces from becoming acholic, the clinical picture is as much one of chronic obstructive jaundice as it is of hepatic cirrhosis. One can also easily understand that (owing to secondary malnutrition and toxæmia) in the later stages of the disease the anatomical features of ordinary multilobular cirrhosis become grafted on those of unilobular cirrhosis; the irregularity of the cirrhotic process may be further increased by the development of nodular regenerative changes in the surviving glandular parenchyma. According to this view some of the features of Hanot's disease are those of cirrhosis of the hepatic parenchyma whilst some are those of exceedingly chronic obstructive jaundice, such as follow occlusion of bile-ducts by experimental ligature or otherwise, or rather, such as would follow occlusion of many of the minute intrahepatic biliary channels by chronic inflammatory changes and plugging with inspissated bile.

4. Chronic Acholuric Jaundice with Enlargement of the Spleen or of Both the Spleen and Liver.

A case of acholuric jaundice simply means a case of jaundice in which no bilirubin can be detected in the urine. In such cases urobilin is usually present in excess in the urine, and the term "urobilin icterus" was used (especially in Germany) to signify the condition in question when it was supposed that urobilin in the blood was the cause of the yellow coloration of the skin and conjunctivæ. Now that bilirubin, though absent (or only exceptionally and temporarily present) in the urine, has been shown to be constantly present in the blood is known to be the cause of the jaundice, the term "acholuric jaundice" or "acholuric icterus" has obviously become preferable to the term "urobilin icterus." Chronic acholuric jaundice is generally accompanied by enlargement of the spleen or both the spleen and the liver. It may occur in early life as a congenital or familial, or both congenital and

familial, peculiarity, or may be acquired in later life. Amongst cases of chronic acholuric jaundice without enlargement of the spleen or liver the series of congenital and familial cases described by Alois Pick¹⁶ is probably to be included. He recorded the case of a strongly built man, jaundiced from birth, who had one brother aged seventeen years, and one sister aged twenty-six years, both likewise jaundiced from birth. In all three the urine contained urobilin but no bilirubin, the faeces were of natural color, and there seemed to be no great, if any, enlargement of liver or spleen. The mother of these three patients, who died when thirty-five years old at her tenth confinement, was likewise said to have been jaundiced from birth.

Chronic acholuric jaundice is nearly always accompanied by more or less decided anæmia, but polycythæmia (excess of red blood-cells) has likewise been recorded. Thus Guinon, Rist, and Simon¹⁷ described the case of a girl, aged ten years, with chronic acholuric jaundice of variable degree, urobilinuria, and chronic splenomegaly; transitory cyanosis and polycythæmia (6,000,000 to 7,600,000 red cells in the cubic millimetre of blood) accompanied an exacerbation of the jaundice. Mosse¹⁸ described the case of a man, aged 58 years, with chronic acholuric jaundice, urobilinuria, and chronic splenomegaly, whose red blood-cells numbered 6,750,000 to 7,825,000 in the cubic millimetre of blood. The anæmia, in the acquired cases at least, may occasionally be of a very severe degree and associated with the presence of megaloblasts¹⁹ in the circulating blood so as temporarily to simulate the blood-picture of pernicious anæmia; the diagnosis of such cases from pernicious anæmia (with enlargement of the spleen) may of course be very difficult. Another difficulty which sometimes arises is to distinguish cases of chronic acholuric jaundice with splenomegaly from cases of splenic anæmia (that is to say, from the adult type of splenic anæmia). It is indeed almost certain that the jaundice

¹⁶ Alois Pick: Wiener klin. Wochenschrift, 1903, No. 17, p. 493.

¹⁷ Guinon, Rist, and Simon: Bull. de la Soc. Méd. des Hôpitaux de Paris, 1904, 3rd Series, vol. xxi, p. 786.

¹⁸ M. Mosse: Deut. Med. Wochenschrift, Berlin, 1907, vol. xxx, p. 2175.

¹⁹ Cf. F. P. Weber: "A Case of Acquired Chronic Acholuric Jaundice with a Blood-picture at One Time Resembling that of Pernicious Anæmia," Medical Society of London, Meeting of February 8, 1909.

may altogether disappear for a time so as to leave the case one of what can be termed "chronic splenomegaly with anæmia" or "chronic splenomegalic anæmia."²⁰ Thus, in the case (Ernest N.) described at the commencement of this paper it is to be noted that the boy himself suffers from a form of chronic acholuric jaundice with splenomegaly and anæmia, but sometimes the jaundice is hardly recognizable by ordinary inspection; moreover one of his sisters suffered from chronic splenomegaly with anæmia without actual jaundice. In other words, it appears almost certain that a form of a "splenomegalic anæmia" without jaundice may alternate with "splenomegalic acholuric jaundice" in the same patient; and it is certain that in a single family one member may be affected with splenomegalic acholuric jaundice and another with splenomegalic anæmia (without jaundice).²¹ On the French "hæmolytic" theory, to which we shall subsequently allude, such cases without jaundice might be classified as representing an incomplete form ("*forme fruste*") of typical ("*complete*") cases with jaundice.

Amongst the clinical characteristics of chronic acholuric jaundice which have been specially investigated by French authors, including Hayem, Gilbert, Lereboullet, Herscher, A. Chauffard, Widai, Abrami, Vaquez, etc., there are several points which we have not yet sufficiently considered. The jaundice, besides being usually very slight, differs also from that of obstructive jaundice in not being associated with bilious urine, acholic fæces, icteric pruritus, or xanthoma. It seems as if a little bile-pigment (possibly without the other constituents of the bile) passes into the blood, scarcely ever, however, in sufficient quantity to give rise to bilirubinuria. Occasionally, however, there may be temporary exacerbations of the jaundice, during which a trace of bile may (as a quite exceptional occurrence) be detected in the urine. According to A. Gilbert, P. Lereboullet, and M. Herscher²² the blood-serum of healthy

²⁰ Cf. Armand-Delille and Feuillié: "Un cas d'anémie splénomégalyque avec fragilité globulaire," Soc. Méd. des hôpitaux de Paris, February 2, 1909, and discussion which followed the exhibition of the case.

²¹ Cf. Chauffard and Troisier: "Des rapports de certaines anémies splénomégalyques avec l'ictère hémolytique congénital," Soc. Méd. des hôpitaux de Paris, February 19, 1909.

²² Gilbert, Lereboullet, et Herscher: Bull. et Mém. de la Soc. Méd. des Hôpitaux de Paris, Séance de 15 Nov., 1907.

normal individuals contains on the average one gramme of bilirubin in 36 litres; but H. P. Hawkins and L. S. Dudgeon²³ say: "The experience of the Clinical Laboratory of St. Thomas's Hospital shows no such frequent presence of bile-pigment in the serum. From an examination of a very considerable number of sera obtained from all possible sources it may be said that bile-pigment is present only in the serum of patients obviously jaundiced or in the serum of patients in whom jaundice is just going to appear." Bile-pigment can always be found in the blood-serum of patients with acholuric jaundice.

The subjective symptoms of these patients are chiefly those of anæmia. Occasionally, however, there may be attacks of abdominal pain or of general depression, lethargy, or drowsiness, accompanied by temporary increase in the degree of the jaundice and sometimes by moderate fever. All the symptoms, as already mentioned, tend to be more severe in the acquired cases in adults than in the congenital and familial cases. It seems as if the cause of the disease (whatever this may be) is more successfully resisted or neutralized in the young patients (that is to say, in the congenital and familial cases that survive) than in patients who acquire the disease in adult life.

The blood-condition in this disease requires special attention. We have already alluded to the nearly constant presence of anæmia and to its variation in degree from time to time according to the severity of the disease; but there are other points which have been specially insisted on by French authors. In the first place there are nearly always a few, occasionally a good many, nucleated red cells to be discovered on microscopic examination of blood-films. These are mostly ordinary normoblasts, but there may likewise be microblasts and in very severe cases (especially in cases of the acquired class) there may be typical megaloblasts present of the "pernicious anæmia" type. The red corpuscles, though fairly normal in shape, vary too much the one from the other in size ("anisocytosis"), and a good many of them usually show polychromatophilia or granular basophilia. The average diameter of the red cells and the color-index are if anything below the normal standard, whereas they are if anything above it in cases of ordinary

²³ Hawkins and Dudgeon: *Quarterly Journal of Medicine*, Oxford, 1909, vol. ii, p. 172.

obstructive jaundice. According to French observations, at least in most of the cases, the red cells show abnormally low resistance to hæmolysis, whereas in chronic obstructive jaundice the rule is for the resistance of the red cells to be above the normal. That is to say, it usually takes a lesser proportion of distilled water to produce hæmolysis in blood withdrawn from these patients with chronic acholuric jaundice than it does in the blood of normal individuals. The abnormal tendency to hæmolysis can be best demonstrated, it is said, when the test is applied to the red cells previously freed from their blood-plasma.

Returning now to the case (Ernest N.) described at the commencement of this paper, we must on the whole regard it as a fairly typical case of splenomegalic chronic acholuric jaundice commencing in early life (probably congenital and familial), though the evidence as to the presence of an abnormally great tendency to hæmolysis is not decisive. It must be acknowledged that a "hæmolytic theory" of the disease, such as was first suggested by Minkowski²⁴ and later on was founded on a firmer basis by A. Chauffard²⁵ and others in France, best suits the facts observed in these cases. One can understand that in addition to the typical cases of chronic (permanent) acholuric jaundice (including those recently described by Hawkins and Dudgeon²⁶ with anæmia and splenomegaly (and possibly hepatomegaly), there are others really of the same pathogeny showing splenomegaly (and possibly hepatomegaly) with anæmia but without jaundice²⁷ or with only occa-

²⁴ O. Minkowski: "Ueber eine hereditäre unter dem Bilde eines chronischen Icterus mit Urobilinurie, Splenomegalie, und Nierensiderosis verlaufende Affection," *Verhandl. des Kongresses für inn. Med.*, Wiesbaden, 1900, xviii, p. 316.

²⁵ A. Chauffard, *Semaine Médicale*, Paris, January 16, 1907, p. 25; and later writings by himself and numerous other observers in France.

²⁶ Hawkins and Dudgeon: *loc. cit.*

²⁷ Armand-Delille and Feuillie: *loc. cit.* The sister of Ernest N. (the case described at the commencement of the present paper) was an example of splenomegaly with anæmia and without actual jaundice, according to Dr. Parkinson's description (already alluded to); but doubtless bile-pigment would have been found present in her blood had it been tested for, as it was later on in her brother's case. Similarly, A. Chauffard and J. Troisier (*loc. cit.*) describe the cases of a mother and son both showing splenomegaly and a blood-picture of "hæmolytic jaundice," but the son is not clinically jaundiced, though his blood-serum contains bile-pigment, just as does that of his mother, who is obviously jaundiced.

sional attacks of jaundice, as perhaps the cases described by Barlow and Batty Shaw,²⁸ and one or more of the family series described earlier by Claude Wilson²⁹ and yet others perhaps showing chronic acholuric jaundice without obvious splenomegaly or hepatomegaly (such as A. Pick's cases already referred to).

Of the pathological anatomy and histology of cases of chronic splenomegalic acholuric jaundice and of the allied cases of "splenomegalic anæmia" without jaundice very little seems to be known, specially in regard to the congenital and familial cases. It is by no means certain that all the cases are identical from the pathological-anatomical and histological point of view. In the congenital and family cases the question may be asked, Is the splenic enlargement ever of the "Gaucher type," that is to say, is it ever characterized by a diffuse growth of the kind of cells which have rightly or wrongly been described as "endothelioid," *i.e.*, cells characterized by a small pyknotic nucleus and apparent excess and unusual transparency of cytoplasm? The Gaucher type of splenomegaly has sometimes occurred in more than one member of the same family, and has moreover sometimes been associated with a yellow coloration of the skin.

In regard to familial cases of chronic acholuric jaundice it seems certain that, though cases of biliary cirrhosis (Hanot's disease) may probably occur in the same family, there is as yet no well-authenticated instance of a typical case of familial splenomegalic acholuric jaundice, or of the allied form of "splenomegalic anæmia," having subsequently developed hepatic cirrhosis and ascites. Therefore the splenomegaly of these families (whether accompanied or not by temporary or permanent acholuric jaundice), though associated with anæmia and constituting a form of "splenomegalic anæmia," must be sharply distinguished from the cases of "splenic anæmia" ("adult splenic anæmia") which ultimately develop hepatic cirrhosis and the symptom-complex of "Banti's disease."

²⁸ Barlow and Batty Shaw: "Inheritance of Recurrent Attacks of Jaundice and of Abdominal Crises, with Hepato-splenomegaly," *Clinical Society's Transactions*, London, 1902, vol. xxxv, p. 155.

²⁹ Claude Wilson: *Clinical Society's Transactions*, London, vol. xxiii, p. 162, and vol. xxvi, p. 163.

DIABETES *

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DIABETES—*diabetes mellitus*—is a disease characterized by glycosuria and hyperglycæmia due to hypoglycolysis, probably from insufficiency of the pancreatic and of the muscular or other glycolytic secretions.

Historically we may infer from the writings of Aretæus, Celsus, Galen and others that they were acquainted with diabetes as a rare affection in Rome in their day. Christie asserts that Cingalese physicians of the fifteenth century spoke of "honey urine." Willis taught at Oxford in the middle of the seventeenth century that the sweetness of diabetic urine was due to sugar, the actual presence of which was demonstrated by Dobson in 1775. The latter also stated that the serum of the blood in his case was sweet; but Ambrosius, in 1835, first extracted sugar from the blood of a diabetic, which others soon after showed to be an excess, rather than a mere presence. Disease of the pancreas with diabetes first appears in the literature with Cawley's report of a case in 1788, which connection has been further developed by Lancereaux, 1877; Von Mering and Minkowski, 1890; Opie, 1901. Rollo, in 1797, advocated a meat diet in the management of diabetes, and Warren, in 1812, extolled the virtues of opium in its treatment. Larrey, in 1820, observed glycosuria following cerebral injury; and Bernard, in 1849, regularly produced this result by injuring portions of the floor of the fourth ventricle. This acute observer also noted, in 1857, the glycogenic function of the liver. Cohnheim, in 1903, demonstrated the interdependence of the pancreatic and muscular glycolytic secretions.

Etiologically you may note that although diabetes is not common, yet it is increasing in prevalence and is an important malady.

* The substance of clinical lectures given in the Cook County Hospital, Chicago, Autumn, 1903.

In the United States it was the cause of death, per 1000 of population, in 1850, 0.009; in 1860, 0.012; in 1870, 0.021; in 1880, 0.028; in 1890, 0.038; in 1900, 0.061. In Prussia, for males, in 1877, 0.007; in 1887, 0.024; in 1897, 0.047; for females, in 1877, 0.007; in 1887, 0.016; in 1897, 0.028. In New York the average for the eleven years, 1889-1899, was 0.094; for the first six years 0.075; for the last five years 0.104. In England and Wales, in 1893, the rate was 0.086; in Paris, in 1891, 0.140; in Malta, in 1891, 0.131. During twenty years 272 diabetics, in 27,721 medical cases, 0.9 per cent., were admitted into the Manchester Royal Infirmary; during seventeen years there were admitted into the Johns Hopkins Hospital 259 diabetics in a total of 106,000 medical cases, 0.25 per cent.

You will find diabetes in all parts of the world, but with especial frequency in Ceylon, Bengal, and other divisions of India; portions of Italy, Germany, Sweden, England, and elsewhere. It is comparatively rare in China and Japan. It is very much more prevalent among the Cingalese, Hindus, and Hebrews than in other races; it is comparatively rare in the negro. It is more frequent in the wealthy than in the poorer classes; in those with mental and sedentary occupations than in those engaged in active physical labor; in males than in females.

In the United States, in 1900, of a total of 4672 deaths from diabetes 2650 were in males and 2022 in females, equal to 57 per cent. and 43 per cent. respectively. In New York, in 1889-1899, there were 936 male to 931 female deaths from this disease. The Prussian statistics are given above. I am of the opinion that, upon a basis of fact, the preponderance of the male sex in diabetes has been frequently overestimated.

Conjugal diabetes has been observed in a small proportion of cases. Oppler and Külz noted it in 47 couples in 3489 cases; Schmidt 26 times in 2320 cases; Schram 45 times in 5000 collected cases; Senator 9 times in 770 cases; I have seen 2 examples.

Diabetes increases in frequency with age, being rare in childhood, commoner in those who have passed over the divide. Of 4655 deaths from this malady in the United States in 1900, there were under 5 years, 150; 5-10 years, 159; 10-20 years, 424; 20-30 years, 377; 30-40 years, 380; 40-50 years, 509; 50-60

years, 709; 60–70 years, 1000; over 70 years, 917. The Johns Hopkins Hospital cases show, 1–10 years, 4; 10–20 years, 14; 20–30 years, 25; 30–40 years, 43; 40–50 years, 68; 50–60 years, 75; 60–70 years, 25; over 70 years, 5. Although diabetes is rare in the young, yet Bogoras collected 486 cases in Russia: Under 1 year, 13; 1–5 years, 92; 5–10 years, 147; 10–15 years, 234. Külz tabulated 111 cases; Stern 117; Wegeli 108. Redon saw 32 cases in his own practice. I have seen only 5 cases in 35 years' practice. Stern reports a congenital case.

Heredity plays a certain, but not large rôle in diabetes. Thus Naunyn obtained a history of diabetes in relatives in 42 of 358 cases; Osler in 6 of 112 cases. Morton, in 1884, observed it in 4 children in one family. Pleasants records 6 cases—2 brothers, 2 sisters, an uncle, and a great-uncle—in the 24 descendants of a common progenitor. Four or more cases in the same family have been seen by many observers. I have seen 3 cases, representing 3 generations, in one family. I have encountered no report of an instance in which a diabetic mother has borne an affected child.

Diabetes has occurred with sufficient frequency to attract attention in tuberculosis, pregnancy, helminthiasis, mental strain, cerebral injuries and diseases, exophthalmic goitre, acromegaly, cholelithiasis, cirrhosis of the liver, ether narcosis, etc.

CLASSIFICATION

Glycosuria and diabetes, you will note, are not synonymous terms, and in this connection the pathogenesis of certain forms of glycosuria may be considered.

It may be said, briefly, that the sugar resulting from carbohydrate digestion is transformed into glycogen, and as such is stored, especially in the liver and muscles, whence it is reconverted into glucose and issued into the circulation as required for assimilation by the various tissues, but mainly and ultimately for combustion, CO_2 and H_2O resulting. By conversion and reversion into glucose and glycogen the issue and withdrawal is so regulated that the blood always contains from 0.1 per cent. to 0.2 per cent. of glucose, and if this proportion is materially increased sugar appears in the urine. The blood contains a glycolytic ferment, which is probably

supplied by the pancreatic islands of Langerhans, and which is effective, or rendered more effective, by complementary secretions, possibly from the muscles. Making use of the sum of your knowledge of the physiology of digestion and metabolism, it must be clear to you that glucose in excess may be present in the blood from (a) failure to be transformed into glycogen and thus slipping through the liver into the general blood current, and failure to be caught up by the muscles and other storage tissues; (b) too rapid reconversion of the stored glycogen into glucose, and its issuance as such from the liver, muscles, etc.; (c) assimilative and, especially, pancreatic, muscular, and other glycolytic failure; (d) cleavage of the protein molecule, sugar resulting.

Alimentary Glycosuria.—Normally the ordinary carbohydrate diet can be employed, and even an excess of from 4 to 8 oz. of glucose equivalent may be taken fasting, without hyperglycæmia occurring. If these, or greater, limits are exceeded glycosuria may appear and persist as long as the dietetic excesses are continued. Under these circumstances glucose is probably offered to the liver, muscles, etc., beyond their capacity for glycogenic conversion and storage capacity, and passes through unchanged. This is the so-called alimentary glycosuria, and to it some persons are always, or at times, peculiarly prone, as are also the subjects of certain diseases, as, e.g., exophthalmic goitre, cirrhosis of the liver, etc. Such persons not infrequently develop genuine diabetes. You should note that in the ingestion of starch the necessary delays of digestion and absorption prevent sudden sanguineous flooding with glucose; and whenever glycosuria follows the taking of starches in any amount, however great, developed or incipient diabetes may be considered to exist.

Nervous Glycosuria.—In Bernard's original and classical experiment irritative injury of the floor of the fourth ventricle was followed by transient glycosuria. As you were permitted to see in the remarkable case from Ward 24, certain traumatic and pathological lesions of this region, and perhaps of other parts of the central nervous system, are accompanied by glycosuria. In these cases the stored glycogen is reconverted into glucose and thrown into the circulation beyond the capacity of normal terminal assimilation and glycolysis. In the absence of a persistent lesion the hyper-

glycaemia and glycosuria are transient. Note, if you please, that in this form of glycosuria the glycogen in the liver and other storage tissues is drawn upon until it is exhausted, with inability to store more, but the proteid tissues of the body are not converted into sugar.

Renal Glycosuria.—Normally the renal epithelium does not permit leakage of sugar, either because of nervous inhibition, or because the sugar is not presented in acceptable form. Certain toxic substances, however, have the power of temporarily deranging this function, with glycosuria as a result. Phloridzin may be taken as a representative of these substances, and when this glucoside is given in sufficient doses transient glycosuria is induced. This glycosuria is due to abnormal excretion, inasmuch as there is no increase of sugar in the blood, on the contrary it is reduced to a minimum. That the morbid process is confined to the kidneys is proven by the experiments of Zuntz, Pavy, and others, wherein the action of the drug was limited to one of these organs. It may be reasonably inferred that functional or organic changes in the renal epithelium are essential to this form of glycosuria, and from all the facts at our disposal we may select one of two hypotheses to explain the facts: (a) that the inhibitory action which prevents the renal epithelium from excreting sugar is temporarily paralyzed; or, (b) that the sugar in the blood is so altered, molecularly, as to be acceptable to the secreting cells. It is clear that although this form of glycosuria might account for some transient cases, it is not operative in diabetes, in which there is a hyperglycaemia as well as glycosuria, notwithstanding the suggestive cases reported by Naunyn, Klemperer, and others.

Suprarenal Glycosuria.—Following the introduction in excess of a solution of the active principle of the suprarenal gland, or even after painting the pancreas with the same, glycosuria with hyperglycaemia appears. It is transient, and is probably due to interference with oxidation within the pancreatic cells of the islands of Langerhans, although it may be due to temporary suspension of the secretion from these cells.

Diabetic Glycosuria.—This is characterized by hyperglycaemia, is persistent under ordinary dietetic conditions, and is probably due to insufficiency of the pancreatic glycolytic secretion, or of its com-

plements. In the severer cases of this form the system is not only drained of its stored glycogen, but glucose is also formed of the ingested and body proteids as well. This subject will be considered further.

ETIOLOGY

The ultimate cause of diabetes has not yet been demonstrated to complete satisfaction. It is probable, however, that it is due to insufficiency of the pancreatic glycolytic secretion, or its complements, or to a lack of harmony between these. The facts upon which we may base a reasonable assumption of this probability are, in part, as follows:

Pancreatic disease may be accompanied by glycosuria and diabetes. The abundant statistical material bearing upon this question is, for the most part, utterly unreliable, in the light of our present-day knowledge; but we may be assured that this will be soon supplied. Diabetes has been observed in some cases of very large cancerous involvement of this organ, although usually absent. Seitz collected a large number of cases with complete destruction of the pancreas by acute hemorrhagic pancreatitis with glycosuria in none. In Nash's case, however, abundant glycosuria developed, with gradual decline during convalescence after operation. Glycosuria was present, for a few days only, in one of my cases. Possibly the time of complete incapacity in these cases is so short that glycolysis continues from materials previously produced. Within recent years there have been found, post mortem, certain lesions of the islands of Langerhans with such frequency that it is probable that it is in an insufficiency of the secretion of these portions of the pancreas that the essential alterations in diabetes are found. Such lesions, or perhaps a functional incapacity, may be due to some long-continued alimentary or intestinal disorder with consequent toxæmia.

Extirpation of the pancreas is regularly followed by diabetes, with all its characteristics. This was first conclusively demonstrated by Von Mering and Minkowski, in 1889, and their conclusions have been abundantly confirmed by numerous experimenters. If a portion of the pancreas, as, *e.g.*, one-fourth or more, varying within wide limits, is left, glycosuria does not follow, or if it does it is transient. If a portion of the gland has been

previously grafted beneath the skin glycosuria does not occur, but if this is later removed diabetes results.

The morbid anatomical findings in those who die from diabetes will differ from those in patients dying with, but not from, this malady, and you should note that the fact is of clinical importance. In the former class the body is usually emaciated; in some cases to an extreme degree. The muscles are remarkably dry; the heart muscle is atrophied, and there may be fatty degeneration. Arteriosclerosis is common, but this is often only an incident of age. Gangrene, especially of the feet, may be present. The lungs are sometimes tubercular—an accidental circumstance. In rare cases, as you have seen, there may be lesions of the fourth ventricle or other parts of the central nervous system. Fütterer found glycogen in the brain and spinal cord. The slightly tumefied liver is darker and harder than normal, with distended capillaries, enlarged acini, and hypertrophied hepatic cells. Cirrhosis is found in the rare cases of hæmochromatosis. The stomach is dilated. The kidneys usually show hyaline degeneration, especially of the epithelial cells of Henle's loop—Armanni's lesion—and other changes are often present.

Anatomical alterations have been found more often in the pancreas than in any other organ. Of the gross changes cirrhotic atrophy has been present in a great majority of cases: Bloch found this condition in 8 of 22 cases; Dieckhoff in 21 of 53; Frerichs in 12 of 40; Hanseemann in 40 of 54; Opie in 15 of 19; Oser in 110 of 188; Osler in 9 of 15; Schmidt in 7 of 23; Weichselbaum and Stangl in all of 18; Williamson in 16 of 24; Wright and Joslin in 2 of 9.

Apparently the most important and significant pancreatic lesions, however, are those affecting the islands of Langerhans, as in chronic interlobular and, especially, interacinar pancreatitis, and hyaline degeneration. The changes which mark the development of these conditions may be briefly mentioned: In the interlobular form duct obstruction is the usual cause. In the most intense grades the interlobular connective tissue is greatly increased and, as bands and strands, surrounds and invades the lobules, with their partial or complete destruction in large numbers, with more or less atrophied acini scattered about. With the contraction of the scar-like tissue

the islands of Langerhans are brought nearer together; later these are compressed and become atrophic, apparently from circulatory failure. In the interacinar form the fibrous infiltration begins in the interacinar spaces, compresses and destroys the acini, and invades the islands of Langerhans, the cells of which shrink and partially disappear. The fibrosis may be, and usually is, much more extensive, affecting also the interlobular connective tissue, with hardening and accentuated lobulation of the gland. Late, fat is deposited in the connective tissue, and is increased about the gland. In hyaline degeneration the islands of Langerhans are specifically selected, and in advanced cases they may be largely unrecognizable. Early the acini are not involved; later they, as well as the blood-vessels, become affected. The hyaline material appears to be a product of cellular degeneration; it stains with the acid dyes, and does not give the reactions of fibrin or amyloid material.

In some cases the pancreas, with our present facilities for examination and knowledge for interpretation, is found macroscopically and microscopically normal. Functional insufficiency, *per se*, can be neither affirmed nor denied. It is probable that future studies will soon clarify this field.

SYMPTOMS

Diabetes almost always develops so insidiously that the patient cannot fix upon the time of beginning. This applies especially to the ordinary case in an elderly person. Very rarely in the aged, but not infrequently in the young, the onset is sudden, and in these cases the course is usually severe, short, and fatal.

The first symptoms to attract the attention of the patient are, usually, nocturnal dryness of the mouth and throat, increased frequency of urination, and excessive thirst. Diabetics who were not aware of the nature of their malady have oftener consulted me because of the first-mentioned of these symptoms than for any other. However, when their attention has been called to the fact they have recognized that polydipsia and polyuria antedated the faucial dryness by a considerable period. In the patient before you the stiffness of the dried soiled clothing first attracted his notice.

A few years ago a patient brought to me a bottle of urine for examination, giving as his reason that the dripping urine left a whitish spot upon his polished shoes; during the year preceding he had developed a voracious appetite, had such thirst that a large pitcher of water was taken during the night, and remarked that a large chamber vessel was filled by his frequent and profuse nocturnal urinations. Recently a patient, found to be diabetic, consulted me for "premature second childhood"—for a few nights he had been wetting the bed. Pruritus, eczema, furunculosis, gangrene, or cataract in elderly subjects, or dryness of the skin, weakness, loss of weight, or sexual impotence in those younger, may lead to the discovery of unsuspected diabetes.

About fifteen years ago an intelligent Hebrew, 40 years of age, whose mother had recently died from diabetes, consulted me for the expressed purpose of discovering whether he was diabetic. There were no symptoms; the urine was free from sugar; he bore glucose to excess without inducing glycosuria. Remaining under my care, with regular urinary examinations, he, some years later, upon learning that a brother had become diabetic, repeated the glucose test with negative results. Routine analyses of the urine were continued. In July, 1908, there was no trace of sugar. Early in September he came to me complaining of sexual impotence. Upon questioning he admitted nocturnal thirst, frequent urination, and dryness of the mouth. The urine contained 1 per cent. of sugar. He is able to take all ordinary foods, including starches and honey, with freedom from glycosuria so long as sugar is avoided. The impotence persists.

Multiple neuritides, and a form of pseudotabes, are not infrequently found to be due to diabetes. Frequently the condition is discovered accidentally in persons supposed to be in perfect health. In this connection, however, I am constrained to say that in my own experience, in an unusually stable clientele, with regular periodic examinations of the urine in a large number of persons who are middle aged or past, I have rarely discovered sugar in the urine unless the patient had presented suggestive symptoms.

The thirst is a quickly returning one, is imperative and uncontrollable. It may be due to a call for water to dilute the sugar in the blood, to facilitate glycolytic hydrolysis, to an effort to wash out

of the system an offending material, to a demand for liquid to replace that lost through the kidneys. The increased flow of urine naturally follows the excessive ingestion of liquids; possibly the glucose stimulates the renal cells to extraordinary activity. In some cases there is neither polydipsia nor polyuria. In these the proportion of sugar is usually small or moderate, and they are readily amenable to treatment. I have, however, seen cases of this kind with sugar present in considerable quantities which persistently resisted a rigid diet. Such cases should be viewed with serious concern.

There is, usually, dryness and harshness of the skin, with absence of perspiration. You will note, however, that in the patient before us perspiration is readily induced, although the case is a severe one, with marked acidosis. Irritation, inflammation, and troublesome pruritus about the genitals are due to bacterial infection invited and nurtured by the glucose-sodden tissues. Furunculosis often occurs; carbuncle may be a late and very serious complication. Wounds, accidentally or surgically made, are especially liable to become infected; they do poorly. Injuries and surgical operations are not infrequently followed by coma. Anæsthetics are not borne well. Gangrene as a late event, in senile cases especially, is a notable contingency; in the great majority of cases the seat is one of the toes, or foot, although it may attack a finger, an ear, the nose, etc.; it may be of limited extent and of the dry variety, or it may be very extensive and moist; it usually follows a trivial injury, or the cause may not be apparent. Arterial degenerations are almost always present, marking a dangerous case.

The appetite is usually good; often it is voracious. Not only are large quantities of food taken at the regular meals, but there is often an urgent demand for food at more frequent intervals, and if this desire is not gratified a peculiar faint and "aching void" sensation in the epigastrium results. The tongue is remarkably clean in some instances; in others it is denuded of epithelium and ulcerous; in yet others it, and the mouth as well, is covered with a sticky mucus. In one case the last-mentioned feature was prominent for several months before sugar was detected in the urine, notwithstanding excessive glucose feeding upon two occasions. The gums may be soft, with necrotic patches; the teeth decay readily.

Gastric eructations and recurrent attacks of mild indigestion may be occasionally seen. Constipation is the rule; diarrhœa, with large stools, is a feature in some acute cases. In mild cases the body-weight is well maintained, and may be even increased, and this also applies to relieved diabetic glycosuria; but in all severe cases, especially in younger persons, there is progressive, sometimes rapid, emaciation, and in the severest cases this may be extreme.

In the advanced stages of severe cases the breath has a peculiar heavy, sweetish, aromatic acetous odor which has been compared to that of stale beer, decaying apples, etc. It is due to acetone, as pointed out by Petters, in 1857. Bronchitis is frequently present. Tuberculosis occurs oftener in diabetics than in others; rarely in the aged; less frequently in this country than in Europe; not so often now as formerly. The lungs of such persons appear to facilitate the lodgment of the tubercle bacillus and to afford a peculiarly favorable soil for its growth. Tubercular cases probably invariably die; certainly I have never seen or heard of an authenticated instance of recovery. Pneumonia, possibly with gangrene, is a very dangerous complication.

Coma is often the immediate cause of death in the advanced stages of severe diabetes. The typical form is that first described by Küssmaul, in 1874, in which there gradually develop restlessness, irritability, weakness, dizziness, digestive disturbances, and hypogastric pain, jactitation, thickness of speech, central amblyopia, possibly retinal and pulmonary hemorrhages, diminution of urinary and saccharine excretion, decline of thirst, appearance of albumin and immense numbers of short hyaline and granular casts in the urine, very rapid pulse with greatly lowered tension, temperature somewhat elevated at first but later becoming subnormal, and a characteristic form of dyspnœa in which the slightly accelerated breathing is remarkably deep and full, loud—audible throughout the room—but without stertor. After few or many of the above symptoms have continued for a very short time to several hours unconsciousness, more or less quickly becoming profound, develops, followed almost always by death in a few hours, or a day or two. This form of coma arises in connection with a more or less profound acidosis, and is probably due to a beta-oxybutyric-acidæmia.

In a certain proportion of cases other forms of coma are encountered, as, *e.g.*, one in which, without dyspnœa, there develop a rapid pulse, vacuity, thickness of speech, and other symptoms simulating alcoholic intoxication, deep coma and death in a short time; another, in which the patient quickly becomes profoundly prostrated, drowsy, has a thready pulse, coldness of the extremities, and gradually developing coma, unaccompanied by dyspnœa, and dies in a few hours. In this form there is absence of acetone odor to the breath, and diacetic acid is not found in the urine. Other anomalous forms may be encountered. Diabetic coma must be differentiated from alcoholism, cerebral affections, uræmia, and other varieties of coma.

Tingling and numbness of the hands and feet, diminution of the tendon reflexes, fleeting acute pains, etc., are often present, and these, with weakened extensors of the feet, and a peculiar steppage gait, may be so prominent as to have given rise to the inappropriate designation of "diabetic tabes." Early impotence usually indicates a severe case. The young and severely affected diabetic is likely to be suspicious, apprehensive, and melancholic. Mental aberration may occur.

Cataract occurs with special frequency in diabetics; it is bilateral, of the soft variety, with lenticular tumefaction and the development of myopia or the lessening of an existing hypermetropia. In the early stages slight opacities may diminish or even disappear with the passing of the glycosuria, but this does not apply to the later stages or the more pronounced lesions. Operations upon the eye should not be made in severe diabetes, but they may be undertaken when nutrition is good and with ability to take a moderate amount of carbohydrates without increasing slight glycosuria and polydipsia. There is distention of the retinal vessels and these may rupture. Amblyopia, retinitis, retrobulbar neuritis, and optic atrophy may occur.

The diabetic woman in the child-bearing period is often amenorrhœic, and she conceives infrequently. Should pregnancy occur abortion takes place in a considerable proportion of cases, usually with death to the fœtus. The puerperium is fraught with especial dangers. The diabetes is likely to be aggravated by pregnancy and confinement. Because the urine of pregnant women is regularly

examined, perhaps for the first time, it follows that diabetes is often discovered at this time. These frequent analyses sometimes lead to the recognition of a transient alimentary glycosuria. Many of the glycosurias of pregnancy and the lying-in are due to lacteal reabsorption, the sugar being lactose, and not glucose. The condition disappears with the adjustment of nursing.

The specific gravity of the blood is increased, as are the red cells and hæmoglobin. There is probably from the first in all cases a tendency toward acidosis, and in the severe case this is measurable, marked, and progressive. It follows that the alkalinity of the blood is reduced, and in the severest cases, with coma threatening or present, this reduction may be very great. The acids which drain away the bases are beta-oxybutyric and its derivative diacetic. In this connection it should be remembered that any quantitative estimation of the reduction of the alkalinity of the blood cannot take into consideration the changes in the cells of the body, and these are probably of greatest importance.

The sugar content of the blood is augmented, from the normal of 0.1 per cent. or 0.2 per cent. to double or triple these proportions. The leucocytes are normal or moderately increased in number and contain glycogen. The red cells stain abnormally with eosin and methylene blue. Smears of dried blood, heated for ten minutes at 135° C., do not stain with solution of Congo red—*Bremner's test*. Diabetic blood decolorizes weak alkaline solutions of methylene blue—*Williamson's test*.

The fat in the blood is increased, with some additions or modifications in its characteristics. In some cases the fat in the blood reaches the most astounding proportions, as, *e.g.*, 18.1 per cent. in Fischer's case. When the proportion is very large the blood is turbid, and grayish or salmon-colored; and when centrifuged a creamy scum overlays the serum. The fat is in the form of minute droplets and actively motile granules; the latter, and probably an extremely tenuous envelope of the former, being probably an ester of cholesterin with a fatty acid. They are only partially dissolved in ether and stain irregularly with osmic acid and with Sudan III.

The carbon dioxide content of the blood is reduced, slightly in the lighter cases to less than one-half the normal in those with coma. The cause of this reduction is not clear; it is not wholly due to

absorptive incapacity of the blood and it probably lies largely in faulty tissue-cellular oxidation.

The urine is almost always increased in quantity, ordinarily ranging, for the twenty-four hours, to from 4 to 6 pints; often it is more; rarely it rises to 20, 50, or 70 pints—amounts which may well tax your credulity; occasionally it is persistently normal, even with a moderate excretion of sugar—as noted by Cawley, in 1788; it is often normal or less under proper diet, during intercurrent affections, with the advent of nephritis, or upon the approach of death. Generally speaking the quantity of urine excreted is from 10 per cent. to 20 per cent. less than that of the liquids ingested, but for short periods this may be reversed, especially in severe cases with rapid emaciation. The necessarily frequent micturition interferes with rest at night and with convenience during the day.

Diabetic urine is usually light in color; often it is pale lemon; rarely it is without color; in mild cases and when the urine is not increased in quantity the color may be normal. When voided it is clear, but soon becomes turbid upon exposure to the air at room temperature, from fermentation; with inflammation of the urinary passages it may be cloudy when passed. The urine is acid. The odor may be normal; in severe cases it often has a sweetish, aromatic, acetous, fruity odor which has been compared to that of stale beer, sweet briar, new-mown hay, decaying apples, etc.; upon fermentation it acquires an acetous or vinous odor.

The specific gravity of the fresh urine will vary with the comparative excretion of sugar, other solids, and water; usually it is high, ranging from 1025 to 1040; sometimes it is very high, as, *e.g.*, up to 1074, as in Bouchardat's and Prout's cases; occasionally it may be reduced by an excess of water and diminution of solids. The chlorides and sulphates, because of dietetic excesses and corporeal waste, are usually increased; there is an excess of phosphates, which is sometimes very great; lime and ammonia are also increased.

Albumin, usually with casts, is present, soon or late, in a very large proportion of the cases. Early, or throughout in mild cases, it may be intermittent and is of no serious import; when it appears late it is generally due to nephritis and indicates a serious condition. In the exceptional case the nephritis may become the most important feature.

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Sugar, in the form of dextrose, $C_6H_{12}O_6$, is persistently present in readily recognizable quantities when the patient is upon an ordinary mixed diet, and this is the one constant and distinctive symptom in diabetes. The amount will vary in different cases from a mere trace to 10 per cent. or 15 per cent., but will vary, upon a uniform diet, within comparatively narrow limits in the individual case. The total amount excreted in twenty-four hours will range from a negligible quantity up to 6 or 8 ounces, and in rare instances to very much more, as, *e.g.*, up to 50 ounces, in Dickinson's case. The excretion will vary with the type of the attack from a mere trace to 2 per cent. or 3 per cent. in the mild cases, to from 4 per cent. to 8 per cent. or more in the severe cases; it may vary with the character of the diet, being less or disappearing upon non-carbohydrate foods; with the time, being less at night and more during the day; with the amount of muscular exertion, being reduced thereby, except in the severest forms of wasting. It may be reduced by proper diet, by acute infections, by nephritis, by approaching coma and death. It may be increased by the excessive ingestion of sugars and carbohydrates in general, by mental worry, etc. In my experience some mild cases have been permanently transferred to the severe class, apparently, by immoderate dietetic indulgences.

TESTS

To detect and estimate sugar in the urine the following procedures may be instituted:

The Specimen of Urine.—In the first instance a specimen of urine should be obtained with the patient upon his ordinary diet. A specimen of the twenty-four hours' urine should be had if practicable, but if this is lacking that of a single passage, preferably about three hours after a meal, may be employed for qualitative testing. The morning's urine, the urine having been previously voided five hours after the evening meal, will exhibit the sugar at its lowest ebb; the urine of three or four hours after various test meals will give information as to the effects of diet; a specimen of the twenty-four hours' urine is necessary for quantitative estimation. This last should be obtained as follows: Save in a clean vessel (preferably one which has been sterilized) all the urine

voided in twenty-four hours (not including that passed at the hour corresponding to the time of beginning), keeping the mouth of the vessel closed with cotton wool. At the end of the period shake the vessel, measure accurately, and take three ounces of the mixed urine and put in a clean and sterilized vial. Label with name, date, and quantity passed in the twenty-four hours. There should also accompany an ounce of freshly voided urine for microscopic examination.

The *tests for sugar* which I have found most satisfactory for routine work are the following:

HAINES'S TEST—Reagent.—Make a complete solution of pure sulphate of copper, 30 grains, in $\frac{1}{2}$ ounce of distilled water; add $\frac{1}{2}$ ounce of pure glycerin and mix thoroughly; add 5 ounces of liquor potassæ.

Test.—Take 1 drachm of the solution in a test tube; gently boil; add up to 6 drops of the urine; gently boil. If sugar is present a copious precipitate of yellowish, or yellowish-red, or red hydroxide or oxide of copper will be noted.

Notes.—The solution is stable and is always ready for use. The boiling should not be too long continued—a half-minute is sufficient. The appearance of a greenish or grayish cloudiness does not indicate sugar. With this test, in common with all those depending upon copper reduction, more or less discoloration occurs in the presence of excessive amounts of uric acid, creatinin, urobilin, glycuronic acid, etc.; also after the administration of salicylic acid, salol, sulphonal, chloral, tannin, gallic acid, alkaloids, etc. True, the discolorations produced by these are not typical, yet they may mislead, and should always lead you to make further investigations.

PHENYLHYDRAZINE TEST.—Reagents.—(1) Phenylhydrazine hydrochloride; (2) sodium acetate.

Test.—In a test tube put 8 grains phenylhydrazine hydrochloride, 12 grains of sodium acetate, $1\frac{1}{2}$ drachms distilled water, and an equal quantity of urine (which has been freed from albumin and filtered); shake well; stand in hot water for half an hour; agitate; cool. If sugar is present there may be seen a deposit of yellow phenylglucosazone, appearing under a $\frac{1}{6}$ " lense, as sheaves and rosettes of needle-shaped crystals.

Notes.—This test has a reliable sensibility to about 0.05 per

cent. of sugar, and is the most delicate of the readily available tests. If the sugar present is glucose the crystals are those of phenylglucosazone, with a melting point of about 205°C ., or as low as 175°C ., if they are impure. The osazone of levulose cannot be differentiated from that of glucose, but that of pentose has a melting point of about 160°C . Glycuronic acid phenylosazone has a melting point of 115°C . Phenylhydrazine should not be allowed to fall upon the hands, as acute dermatitis will result.

RUBNER'S TEST.—*Reagents.*—(1) Acetate of lead, saturated solution; (2) ammonium hydroxide.

Test.—Dilute the urine to a specific gravity of 1010. To 10 c.c. of the diluted urine add an equal quantity of the acetate of lead solution; filter; to a portion of the filtrate, in a very narrow test tube, add, drop by drop, ammonium hydroxide until a heavy white precipitate of lead saccharate is formed; apply gentle heat, not to exceed 80°C .; if glucose is present the precipitate assumes a pink color, or a darker shade of red, the color fading somewhat upon cooling.

Notes.—This test does not react typically with any other substance. Glycuronic acid produces a similar, but not identical reaction. The coloration which may occur with indoxylsulphuric acid in large excess is not readily mistaken for that of glucose.

The above qualitative tests will demonstrate the presence or absence of sugar. The *absence* of sugar may be determined by the proper application of any one of these, of which Haines's, with a sensitiveness of 0.3 per cent., is the most convenient and generally useful. In examining a patient for the first time, or after the lapse of several months, the phenylhydrazine test, because of its extraordinary sensitiveness, should always be employed. The *presence* of sugar should, as a rule, not be predicated upon the positive reaction of a single test. If Haines's or the phenylhydrazine test gives a reaction, you should confirm it by Rubner's, which has a reliable sensitiveness of 0.2 per cent., and has fewer disturbing factors to encounter than any other.

To determine the quantity of sugar present the following tests are most reliable:

FERMENTATION TEST.—*Reagent.*—Compressed brewers' yeast.

Test.—Three ounces of saccharine urine are put into an 8 oz. bottle; add $\frac{1}{4}$ cake of yeast; shake; close mouth of bottle with cotton wool or a nicked cork; set in a warm place. Beside this place 3 ounces of the same urine, without yeast, in a tightly corked vial. After about twenty-four hours take, separately, the specific gravity of the contents of the two vials; subtract the sp. gr. of the fermented from that of the unfermented urine; every degree of density lost represents 1 grain of glucose per fluidounce, and this multiplied by 0.22 will give the approximate percentage.

Notes.—This test is sensitive to about 0.5 per cent. of sugar, and as you well know is more reliable than any other. Its disadvantages are that about twenty-four hours' time is required, and that its action may be interfered with by inactivity of the ferment, and by salol, salicylic acid, urotropin, and some other drugs which may have been taken by the patient, or introduced into the urine.

PURDY'S TEST.—*Reagent.*—Dissolve 4.752 Gm. pure sulphate of copper in 200 c.c. distilled water, with gentle heat; dissolve 23.5 Gm. potassium hydroxide in a sufficient quantity of distilled water; mix these two solutions; cool; add 350 c.c. stronger ammonia, U. S. P.; add 38 c.c. pure glycerin; add distilled water to make 1000 c.c.

Test.—Take 35 c.c. of the test solution and an equal quantity of distilled water; put in a small flask, as, *e.g.*, one of 150 c.c. capacity; bring to and maintain at the boiling point, with ebullition; into the boiling solution the urine to be tested is discharged from a finely graduated burette, drop by drop, until the blue color begins to fade, then more slowly, allowing three or four seconds to elapse between the drops, until the blue color entirely disappears. It requires 0.02 Gm. of sugar to decolorize the 35 c.c. of test solution, and this amount is contained in the quantity of urine required to complete the test and the percentages may be calculated upon this basis.

Notes.—The test solution is stable. In testing no precipitate is thrown down, the cuprous hydroxide being held in solution by the ammonia. Urines which contain much sugar should be diluted with distilled water, *e.g.*, one volume of each, and the result multiplied by 2; or 3 volumes of water to 1 of urine, and the result

quadrupled. The following table will facilitate the finding of the percentages:

Reading of burette.	Per cent. of sugar.	Reading of burette.	Per cent. of sugar.	Reading of burette.	Per cent. of sugar.
0.4 c.c.	5.0	0.9 c.c.	2.2	4.0 c.c.	0.5
0.5 c.c.	4.0	1.0 c.c.	2.0	5.0 c.c.	0.4
0.6 c.c.	3.3	1.5 c.c.	1.3	6.0 c.c.	0.3
0.7 c.c.	2.9	2.0 c.c.	1.0	8.0 c.c.	0.25
0.8 c.c.	2.5	3.0 c.c.	0.7	10.0 c.c.	0.2

The decolorized solution employed in making the test will resume a bluish color after standing for a time; this is due to reoxidation and not to imperfect reduction. The contact of the air with the surface of the solution during the short time required to make the test does not materially affect the result. This test, introduced by the late Dr. Purdy as an essential modification of that of Pavy, is sensitive to 0.3 per cent., and is the most convenient and generally useful quantitative test for urinary sugar known to me.

For details concerning the many other tests for sugar in the urine, including that by polarimetry, which is the most sensitive of all, but is lacking in availability; and that of Fehling, which is the most popular, you are referred to special treatises and to the periodical literature.

Late in severe cases of diabetes the body proteid tissues disintegrate and are eliminated, mainly as nitrogen, in the form of urea and ammonia, and sugar, the latter forming about 60 per cent. of the products of this destructive metamorphosis. Not all of these, however, range themselves in the above classes, but are to be found in the acetone series of products, as acetone, diacetic acid, and beta-oxybutyric acid, loading the blood and serum of the body and finding their exit mainly by the urine.

Acetone in the urine of diabetics indicates a serious condition. It may be recognized as follows:

LEGAL'S TEST.—*Reagents.*—(1) Sodium nitroprusside; (2) 10 per cent. solution of sodium hydroxide; (3) acetic acid.

Test.—Take 10 c.c. urine; add a small fragment of sodium nitroprusside; shake; add 1 or 2 c.c. of the sodium hydroxide solution; a cherry-red color is produced which soon fades; add acetic acid to excess. If acetone is present a carmine or purplish-red color is developed.

Notes.—Previous distillation of the urine is advisable, and may be necessary. The red color may be of various shades. Creatinin is excluded by the acetic acid.

In the more severe cases diacetic acid is present in the blood and urine. It is only found in those cases in which its conversion into acetone is incomplete, and probably indicates a more rapid disintegration of the body tissues. In significance it stands in gravity between acetone and beta-oxybutyric acid. It may be detected in the urine as follows:

GERHARDT'S TEST.—*Reagents.*—(1) Ferric chloride solution, 10 per cent.; (2) sulphuric acid.

Test.—Take 10 c.c. of fresh urine; add, drop by drop, ferric chloride solution until the white precipitate of ferric phosphate, which first appears, is dissolved. A deep red or port-wine color is produced if diacetic acid is present. The color fades if sulphuric acid is added.

Notes.—A similar reaction, which will not deceive the practised eye, occurs in the urine of a person who has been taking antipyrine, salicylic acid, etc. In such cases you will find the reaction for acetone confirmatory, inasmuch as this substance is always present when diacetic acid exists.

The presence of beta-oxybutyric acid is of the gravest importance, as when once it appears it remains more or less permanently. In extreme cases it may be eliminated by the kidneys in very large quantities; 1 or 2 oz. per day is not uncommon; 3 to 5 oz. may be encountered; up to $7\frac{1}{2}$ oz. have been recorded. When you consider that much of the beta-oxybutyric acid, resulting from the incomplete or faulty combustion of fats, is converted into diacetic acid and acetone, substances which we cannot accurately measure, the tissue waste represented by these high readings must be enormous. Beta-oxybutyric acid is lævorotatory and may be recognized and estimated as follows:—

POLARISCOPE TEST.—*Apparatus.*—Ultzmann's polarizing saccharometer.

Test.—Take polariscopic reading of urine in percentage of sugar; also estimate, by the fermentation or Purdy's test; subtract result obtained by polariscopy from that obtained by one of the

others; the difference will represent, approximately, the percentage of beta-oxybutyric acid. Confirm by making the polariscopic test directly upon the fermented urine.

Notes.—No test for beta-oxybutyric acid is necessary unless acetone and diacetic acid are present. With these derivatives present there is no other substance which is lævorotatory, which in practice you need consider, except beta-oxybutyric acid. If the urine is dark or turbid, or contains albumin, these disturbing factors should be removed by adding to 20 c.c. urine 5 c.c. saturated solution of acetate of lead, and filtering. Use the filtrate and correct the result by adding 25 per cent.

In the vast majority of cases diabetes is a very chronic affection. Beginning in late middle life it usually continues, an incurable but fairly controllable disease, until early or even late old age, with death from ordinary causes, probably modified by the hyperglycæmia. My oldest patient died at 89, of pneumonia, having had knowledge that diabetes was present for more than 25 years, and with a strong presumption that the actual duration was much longer. It is my opinion, based upon a fairly large experience with the disease, that, in the class of cases above mentioned, and under proper management, the duration of diabetes is, practically, indefinite, the patients living their days out and dying from some other cause. Although this is true of the average case in those past the middle of life, it does not apply to those who are young, or the severe cases in early middle life, in whom the duration is usually short, or only moderately prolonged. Cases have been reported with a duration of only a few days or weeks. In these it is probable that the true duration has been often underestimated. In adults in the third or fourth decade the duration is usually decidedly longer than in childhood or youth but it lacks the indefinitely prolonged duration noticeable in those who are older. In some mild cases, even in middle life, or somewhat younger, glucose may disappear from the urine for many months at a time, even with a mixed diet, including small amounts of sugar, to reappear with immoderate indulgence, or with mental or physical depression. I have under observation one notable example of this form, in a man of 48, in whom glycosuria was first detected about 18 years ago.

DIAGNOSIS

The diagnosis of diabetes includes the determination of the presence of the disease, its typical characters, and its therapeutic possibilities and requirements. Recognition of the presence of the disease is based, positively, upon the discovery of sugar in the urine, persistently, when the patient is upon an ordinary mixed diet, including a reasonable amount of carbohydrate foods. Dryness of the mouth and throat, immoderate thirst, frequent and free passage of urine, pruritus and irritation of the genitalia, wasting with free ingestion of food, etc., may lead to an examination of the urine in those who do not submit their urine to regular periodic examination.

It is not enough, however, to prove the absence of sugar in the case of a person suspected of having diabetes, because in some persons glycolysis is worked so near to its limit of capacity that they are distinctly upon the border-line and are at any time liable to become confirmed diabetics. In these it is necessary to inform ourselves definitely upon this point by testing their glycolytic capacity. For this purpose daily increasing doses of glucose may be given, with corresponding examinations of the urine, until the limit of capacity has been attained, or until it has been made clear that a normal capacity exists. Again, if sugar is discovered in the urine diagnosis must be reserved until the case has been placed in its proper typical classification. Those cases in which the sugar disappears from the urine with abstinence from sugar and a moderate restriction of other carbohydrates may be classed as mild; those in which glucose persistently continues to show in the urine with a rigid non-carbohydrate diet must be classed as severe. Between these, and modified by age and a great variety of circumstances, lie the subclasses.

The therapeutic diagnosis measures the glycolytic capacity of the patient at the time of the test, and is of paramount importance. This may be best considered in connection with treatment.

PROGNOSIS

Diabetes is, broadly speaking, an incurable disease. In the aged the vast majority of cases are mild, but they do not recover; they live moderately long lives and usually die of maladies not directly

connected with diabetes, although the latter may exert an unfavorable influence; they die with, but not necessarily from, diabetes. Complications, as, *e.g.*, carbuncle, gangrene, etc., carry off a certain proportion of cases. Rarely, in senility, may acute and quickly fatal cases be observed. In the young it is fatal, with a comparatively short duration. In young adults the course is longer, but the ultimate result is, with rare exceptions, the same. The exceptions to this rule you will find in those peculiar cases in which glycosuria is intermittent, with abeyance upon a moderately restricted diet, and reappearance with immoderate indulgence in carbohydrates, or without apparent cause. They do not recover; they may continue indefinitely; they may be transferred to the severe class at any time.

TREATMENT

Diabetics do not recover under treatment, yet with a clear conception of its possibilities their proper management is, upon the whole, fairly satisfactory. In mild cases, which constitute the majority, the patient can be made moderately comfortable and his life indefinitely prolonged.

To obtain these results knowledge and appreciation of certain fundamental factors is essential. You must be broadly and minutely informed upon diabetes, and upon nutrition and waste. You must make, with persistently maintained interest, a special study of the individual case. You must obtain and retain the confidence of your patient; and in order that this may be accomplished it is necessary that he be taken into your confidence, regarding the natural course of the disease, its duration and principles of management, together with the progress of his case from time to time. You must formulate, from your own knowledge and experience, a well-considered and available plan of management, and pursue it, with modifications to meet the requirements of the varying conditions of your patient and his environment, and of your advancing knowledge, without vacillation, throughout the course. You must be lucid and minutely methodical in your directions to the patient. You should appreciate the hopefulness of the problem, if warranted, and convey this, undiluted and in large measure, to your patient; you must be untiringly assiduous and patiently tactful, month after month and year after year, to the end. Probably in no other

malady will you, as physicians, have a better opportunity to feel, and to show, that you are masters of the art of medicine.

Inasmuch as the treatment of diabetes is almost exclusively dietetic, certain fundamental facts concerning foods, nutrition, and waste demand cursory consideration in this place:

By common consent the energy resulting from oxidation changes in the body is measured by the unit value of the calorie. To maintain metabolic equilibrium in a healthy adult of medium size food is required which represents from 2000 to 2500 calories per day, equivalent to from 30 to 35 calories per kilogram of body weight. The various classes of foods have caloric unit values, approximately as follows: Proteids, 4; carbohydrates, 4; fats, 9; alcohol, 7. To meet the requirements of normal metabolism upon the above basis foods of the various classes may be given, to the caloric equivalent without any fixed plan, usually following the dictates of the appetite; or they may be apportioned to meet the individual necessities. The following represents an ordinary well-balanced dietary:

Carbohydrates	350 to 400 Gm.	= 1400 to 1600 calories.
Proteids	75 to 100 Gm.	= 300 to 400 calories.
Fats	35 to 55 Gm.	= 300 to 500 calories.
<hr/>		
Totals	460 to 555 Gm.	= 2000 to 2500 calories.

Usually more food is ingested than is required, the excess being in part stored up as fat and in part discharged along with the waste matters of the body. If, however, materially less than is demanded by the metabolic requirements is persistently taken, the body tissues are drawn upon for oxidation and loss of weight is the result.

In the management of diabetes it is convenient to have a series of typical diet lists, to be readily modified to meet varying requirements. Those which I employ, with the above-mentioned limitations, are as follows:

Diet List "A."—"Diagnostic."—Take fresh meats of all kinds, including, beef, mutton, pork, etc., except liver; game and fowl of all kinds, except goose liver; fish of all kinds, except oysters; fats and oils, including butter, solid cream, and table oil; meat broths, and clam broth; gelatin jelly, flavored with oil of lemon and citric acid and sweetened with saccharine; tea and coffee, with solid cream and saccharine; water and carbonated waters. Sugars and starches

in every form, and all foods not mentioned in this list, must be avoided.

This is my standard basic diet for therapeutic diagnosis. It may be prescribed in any mild case, in the absence of acetone or other form of acidosis. In severe cases, or in any case with any evidences of acidosis, the same result may be obtained by gradually reducing the amount of carbohydrate food and approaching the diet from the opposite end. Ordinarily the patient may select from this list of foods according to his taste or fancy. In some cases, where exactitude is required, specific quantities of the different foods, or classes of foods, may be ordered, always bearing in mind that food in excess of the calculable needs of the patient will be required in those with a considerable excretion of sugar.

Diet List "B."—"Strict Routine Diet."—Take fresh meats of all kinds, except liver; game and fowl of all kinds, except goose liver; fish of all kinds, except oysters; fats, including bone-marrow, oils, butter, cream, etc.; cheese, buttermilk, soured milk, curds, fermented milk; broths and soups made from meat, heavy cream, and vegetables, without starchy thickening; gelatin jelly, flavored with lemon juice and sweetened with saccharine; eggs in every way, except omelette; nuts of all kinds, except chestnuts and peanuts; fresh vegetables, including spinach, cabbage, cauliflower, Brussels sprouts, string beans, tomatoes, young onions, asparagus tips, celery tops, lettuce, cress, dandelion, cucumbers, dill pickles, etc.; acid fruits, including lemons, limes, apples, cherries, olives; such liquids as tea, coffee, water, carbonated and saline waters; whisky and brandy, if required; foods may be sweetened with saccharine; heavy cream may be used. Starches and sugar in every form must be avoided, also all foods not specifically mentioned.

This is my routine diet for severe cases, without acidosis. This list does not exclude every form of carbohydrate, yet it is as strict a diet as can be continued for any length of time by the diabetic.

Diet List "C."—"Moderate Routine Diet."—Take fresh, salt, and cured meats of all kinds, including beef, corned beef, dried beef, tongue, mutton, pork, sausage, ham, bacon, salt pork, tripe, etc., except liver and sugar-cured meats; game and fowl of all kinds, except goose liver; fresh and cured fish of all kinds, except oysters; fats and oils of all kinds, including butter, cream, table oil, etc.; broths

and meat, vegetable, and cream soups of all kinds, without starchy thickening and sweetening; gelatin and Irish moss jellies, flavored with fruit juices or acid wine and sweetened with saccharine; eggs in every form, except as omelette; milk, buttermilk, soured milk, fermented milk, and cheese of all kinds; fresh vegetables, including spinach, cabbage, cauliflower, Brussels sprouts, onions, soft green corn, mushrooms, celery, radishes, lettuce, cucumbers, pickles, chow-chow, cress, tomatoes, etc.; acid fruits, as, *e.g.*, lemons, apples, cherries, strawberries, gooseberries, currants, etc.; tea, coffee, water, carbonated and saline waters; brandy and whisky, if required; cream and saccharine may be used. To the above add a piece of bread or toast, three times a day, amount as especially directed. For the bread or toast there may be substituted, in whole or in part, potatoes, rice, oatmeal, cereals, etc., as may be specifically directed only. Sugar in every form must be avoided. Starches, except as specifically mentioned, and all foods not included in this list, must be avoided.

This is my standard diet, modified to meet individual requirements, in mild cases, and in those severe ones with acidosis. The amount of bread, potato, and other starchy foods allowed must be specifically noted in each case, as well as the period of time for which the diet is prescribed.

The therapeutic diagnosis should follow immediately the discovery of the presence of diabetes. With the patient upon an ordinary mixed diet, including a moderate amount of carbohydrates, a quantitative analysis of the twenty-four hours' urine should be made and the result recorded. This should be fairly complete, with especial reference to quantity, color, sugar, urea, diacetic acid, and evidences of nephritis. The patient should now be placed, at once in the ordinary case, gradually if diacetic acid is present, upon diet list "A." This diet should be continued, with daily urinary analyses, until sugar is no longer present, or until it declines no further and it is evident that it cannot be made to disappear. In either of these contingencies the information may usually be obtained within a week, often within three or four days; rarely will eight or ten days be required. With the disappearance of the sugar, or its reduction to a minimum, you should add to the diet a piece of bread $2 \times 3 \times \frac{1}{2}$ inches, approximately 12 Gm., three times a day

for three days, with daily analyses of the urine. At the end of this period the amount of bread should be further augmented for each three-day period, with corresponding urinary examinations, until glucose reappears in the urine, or its quantity increases, that is, until the patient's glycolytic capacity has been reached. The underlying principles involved in this proceeding must be adhered to in every instance; the details you may vary to meet the requirements of the individual case, or your own fancy.

The dietetics of diabetes is by far the most important part of the management. The objects sought are, to prevent the appearance of sugar in the urine, or its reduction to the least possible amount compatible with the best interests of the patient, with especial reference to the maintenance of his strength, weight, and nutrition at the highest attainable level.

The ordinary mild case should be placed upon the "moderate routine diet," as given in list "C," with a specified quantity of bread to be taken three times a day, which should be as little below the patient's glycolytic capacity as safety will allow. As a rule he may, with a few simple suggestions from you, select from the list those foods which he fancies; rarely will it be necessary for you to specify the quantities of the different classes of food in order that he may obtain the requisite number of calories. The twenty-four hours' urine should now be examined once a month; in exceptional instances every fortnight, or every six or eight weeks. In those cases in which the border-line between the mild and severe is approached, it may be well to introduce, once a week, as a fast day, the more rigid diet of list "B." The patient should be instructed to report to you promptly any increase of thirst, excretion of urine, dryness of the mouth or throat, or other significant symptoms. Three or four times a year the therapeutic diagnosis should be repeated, in order that the diet may be readjusted and that the patient may be given the benefit of the increased tolerance to sugar resulting from the diet to which he has been subjected, and of the few days of stricter diet of the testing period.

Some of the mildest cases bear with impunity a diet restricted only by the exclusion of sugar. These, however, require the same careful management and supervision accorded those of a more severe type; indeed they have been, in my experience, more intractable, as

patients, than the ordinary. These not infrequently become careless, commit dietetic excesses, and pass along to a more severe type.

Some cases, apparently of a mild type but actually belonging to one more severe, can take the diet mentioned, but will be unable to bear any addition of starchy food. For these the diet is sufficiently liberal to allow its continuance indefinitely without its becoming unbearably irksome. In a fair proportion of these cases you may expect slight or even notable improvement in their glycolytic capacity as time progresses.

The severe cases will require the strict routine diet of list "B." In not a few of these it will be necessary for you to add selected foods, including carbohydrates, from list "C," but they should be always specifically mentioned, and with particular reference to quantity. In this type the patient should be allowed considerable latitude of choice, but in the major proportion it will be necessary for you to indicate, closely and clearly, the quantities to be taken of the different classes of foods, in order that their caloric value may meet to the utmost the corporeal tissue requirements. Especially will it be advisable to push the fats to the patient's capacity in this direction. With careful oversight in the selection of fats, their palatable preparation, and inviting presentation, large quantities may be ingested and because of their high caloric content go far in furnishing the full measure of caloric needs of the system. Here also may alcohol find a useful place. In these cases you must remember that it is not enough to supply foods to meet the theoretical requirements of the patient; his practical needs will be your problem. Additional quantities must be given to meet the loss represented by the proteid destruction, measured by the excess of glucose excreted with the urine, above that supplied by the food.

For example, a patient of average size, upon the strict routine diet, voids 4000 c.c. of urine, containing 4 per cent. of glucose. Assuming that his food requirements are 2240 calories, this may be met by, *e.g.*, 300 Gm. proteids = 1200 calories; 100 Gm. fats = 900 calories; 20 Gm. alcohol = 140 calories, making a total of 2240 calories. You will note, however, that 160 Gm. of sugar have been excreted with the urine, equivalent to 540 calories, and that there is, therefore, a metabolic deficit of this amount, which has been obtained, necessarily, by destruction of body tissues. To

maintain a metabolic equilibrium in all such cases it is necessary to furnish food in caloric value in excess of the calculable normal requirements of the individual, plus the caloric value of the sugar voided. In the case under consideration the required excess must be supplied by additional proteids, or carbohydrates, inasmuch as the fats are already being consumed to almost the limits of ordinary tolerance, and the alcohol to the boundary line of prudence. Fortunately this can be done, as the average person may, by the employment of reasonable tact, ingest and assimilate 600 Gm. or more of proteids, with a caloric value of 2400 calories, giving a clear margin, above theoretic requirements and glycosuric loss, of 600 calories, which may be available for dietetic variety.

In severe cases of long standing there will arise the question of relaxing, somewhat, the dietetic stringency and giving the patient small or very moderate amounts of carbohydrates. Experience has abundantly proven that this is highly desirable in certain cases, and absolutely necessary in others. In the last class coma may be averted; in the first the patients cease to lose weight rapidly, gain strength, feel better, and with the increased ingestion of sugar-making foods the saccharine output may not be increased, or if so, not to the full amount represented by the added carbohydrates. The true explanation probably lies in the fact that in these cases the sugar is largely drawn from the body tissues; the addition to the diet of the carbohydrates checks, somewhat, this destructive metamorphosis and appears to stimulate glycolysis. Such dietetic modification should be made, tentatively, in every advanced severe case—indeed you should discreetly anticipate necessity in this matter—and continued to a greater or lesser extent, or discontinued, according to the effects produced. To be sure, you should carefully adjust the amount of carbohydrate to meet the requirements of the individual case; the rule being to introduce the largest amount of this class of food that the patient can bear without increasing the sugar output materially, while at the same time the body weight is maintained and improvement induced in other directions.

For example, a patient of this class voids 3000 c.c. urine, containing 5 per cent. of sugar, equivalent to 150 Gm., or 600 calories. There is now added to the diet 200 Gm. carbohydrates, with a caloric value of 800; the urine is increased to 3500 c.c., with 5 per

cent. of glucose = 175 Gm. = 700 calories. It is clear that in this extreme case the carbohydrates introduced were oxidized to the extent of 700 calories, inasmuch as the output of sugar was increased only 25 Gm., having a caloric value of 100.

Whenever diacetic acid is present in the urine, with or without evidences of impending coma, this change in the diet should be made.

A number of substitutes for bread have been proposed and used. Of these gluten bread has been most popular. It is possible, by repeated careful washings, to make, commercially, a flour composed largely of gluten, and such flours may be procured in this country and abroad. It is, however, of low caloric value, unpalatable, and patients soon tire of it. Nearly all of the alleged gluten flour upon the market is fraudulent, being in fact composed to a large or even a major extent of starch. For these reasons I do not indiscriminately advise these breads; I sometimes allow the best procurable gluten flour to be used, under close supervision, until the patient tires of it. Breads, etc., made from almond meal, desiccated and powdered cocoanut, casein, etc., with the sugar removed, may be used, but of these the patient soon tires.

Some advanced severe cases are able to assimilate small or moderate quantities of levulose, lactose, mannite, etc., and can be given these, as fruit, milk, honey, etc., with benefit. Trial is the only means of judging of their usefulness in the individual case. Should you find that some mild cases can take these with impunity, or that other severe cases are benefited by them, they should be, under these circumstances, advised. As a rule, however, none of these are safe substitutes for ordinary sugar. Saccharine may be used for sweetening foods and drinks. Although harmless it is most satisfactory when used in small quantities. It comes in tablets of convenient size, *e.g.*, $\frac{1}{4}$, $\frac{1}{2}$, and 1 grain each.

Water plays an important rôle in diabetes. It is the solvent for the sugar and the vehicle by which it is eliminated. Nature probably calls for the necessary amount of fluids, and the thirst of the patient should be fairly satisfied, regardless of the quantity required. Some mineral waters have obtained an empirical reputation for usefulness in diabetes; those of Carlsbad, Vichy, and others may be mentioned. These saline waters probably are beneficial—

if they are so—because of their alkalinity, and of their purgative qualities. Of the natural waters of this country the laxative salines of Saratoga are the best. It is to be remembered that the patient will do as well upon artificial salines as upon the natural water. Waters which are carbonated, and which contain a considerable proportion of alkaline carbonates, are theoretically and practically useful. They probably assist in glycolysis and in increasing the alkalinity of the blood.

Constipation is best relieved by some of the natural or artificial saline laxative waters, or by solutions of the citrate or sulphate of magnesium, phosphate or sulphate of sodium, etc.; or by some of the vegetable cathartics.

Moderate but somewhat long-continued active exercises should be taken daily. This I consider of prime importance. Experiments conclusively prove that glycolysis is stimulated by muscular activity, and experience has anticipated and abundantly confirmed the theoretical conclusions which may be drawn therefrom in favor of muscular exercise in diabetes. In patients who are too weak to take much exercise moderate massage may be substituted. In either event I am in the habit of specifically directing the amount and character of the exercise to be taken by the individual. Exercises which bring into play the greatest number of the muscles of the body are most suitable. If practicable the exercises should be interesting and pleasurable; out-door exercises are preferable to those in-doors, but if circumstances make the latter necessary the ventilation should be especially good.

Other miscellaneous features of the hygienic management are important. Out-door occupations are to be preferred. If choice can be had the patient should reside at a low elevation and in a warm climate. The clothing should be comfortable, and that next the surface might well be of silk or wool. A cold, or very hot, salt-water sponge bath should be taken every morning; a hot tub bath may be taken, at night, two or three times a week. The teeth and mouth should be thoroughly cleansed night and morning; the mouth should be rinsed after each meal. The urethral orifice and the surrounding parts should be carefully washed and dried after every urination; the vulva and the glans penis should be frequently bathed. Should irritation, pruritus, or eczema develop upon the

surface, here or elsewhere, you may direct the application of weak solutions of boracic acid, carbolic acid, lead acetate, carbonate of sodium, corrosive chloride of mercury, etc., or ointments of oxide of zinc, etc. In my hands one of the most satisfactory applications for the relief of the heat and itching in these cases has been a 5 per cent. solution of antipyrine.

Furunculosis, carbuncle, and gangrene must be treated upon general surgical principles. Should one of these conditions develop the general management should be accorded the most careful consideration.

In the medicinal treatment of diabetes only one drug—opium, with codeine as the favorite alkaloid—has maintained a reputation for usefulness. There can be no doubts regarding the benefits which some patients derive at times from codeine; thirst and hunger are reduced; polyuria and glycosuria decline; sleep is improved; glycolysis is stimulated; strength and weight are augmented. The increasing constipation and lessening of the appetite are the price paid for the benefits. The dose should be $\frac{1}{4}$ grain gradually increased to 1 or 2 grains three times a day. If the sugar disappears, or is materially diminished, or if no impression has been made after a reasonable time, the codeine should be reduced or suspended. It should be reserved for the severer cases; the mild ones do not require it. In my practice it has been employed but rarely.

Other remedies in great variety have been more or less highly recommended, but none have met with any popular approval. Of these there may be mentioned arsenic, especially the bromide; the bromides generally; creosote and carbonate of creosote; iodides and iodoform; jambul; lactic acid; lithia salts; salicylic acid and the salicylates; strychnine; sulphonal I have used with some benefit. Specifically pancreas, fresh and in the form of various extracts, has been advocated and used, but with indifferent success. Extracts of the pancreas and muscles, with hæmoglobin, is a late proposition. Attempts have been made to graft sheep's pancreas into diabetics, but none have been successful.

Coma is the dreaded complication of severe diabetes. It is usually preceded by a more or less prolonged period of acidosis, during which time the most painstaking prophylactic measures should be instituted. These lie along the lines of frequent and

close observation; the avoidance of making radical changes in the diet, especially in the sudden withdrawal of carbohydrates; the addition of carbohydrates to the diet in those cases upon a rigid diet free from these foods; removing fats from the diet; the systematic use of alkalies, especially the carbonate of soda, given frequently in such doses that from 120 to 180 grains are taken during the twenty-four hours and with the free use of water; the free movement of the bowels. In a few cases I have practised, at intervals, free bleeding, and with apparent benefit. In the milder cases of acidosis, with only moderate excess of ammonia output, you will be well recompensed for the care and attention required for any efficient prophylactic measures which you may institute; in the very grave and rapidly advancing cases of acidosis your efforts will probably fail, but this should only lead to redoubled efforts. From first to last let me urge that your treatment be carefully planned and aggressively followed.

With the actual development of coma the patient should be bled 24 to 32 ounces; an equal amount of a 2 per cent. solution of bicarbonate of soda in normal salt solution introduced into one of the median basilic veins, and this repeated in a few hours; a stronger solution should be introduced into the rectum, preferably by slow infusion, or as an enema, and this latter repeated at intervals of three or four hours; if the patient can swallow a similar solution should be given by the mouth, the object being to saturate the liquids of the body with the alkali as quickly as possible. Oxygen gas may be administered during this time. All these measures should be repeated, continued, suspended, or modified as indicated by the progress of the case. It is fair to say that these measures, attended by distinctly beneficial effects as they are, are uniformly unsuccessful, as measured by the final result.

Surgery

CONGENITAL IDIOPATHIC DILATATION OF THE COLON (HIRSCHSPRUNG'S DISEASE)

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THIS communication is based on two cases of congenital idiopathic dilatation of the colon involving the rectum and sigmoid, one of which I successfully excised and in which I made an end-to-end anastomosis; the other died while being anæsthetized and was found to be the subject also of status lymphaticus. I will give the record of the cases first and then discuss the condition generally.

M. M., *ÆT.* TWELVE YEARS, FEMALE

FAMILY HISTORY.—Mother and father and other children normal.

PREVIOUS ILLNESSES.—None.

HISTORY.—When two or three days old (January 8, 1896) was admitted under Mr. Battles' care into St. Thomas's Hospital, where "the anus was found to be imperforate. A septum one inch from the anus was perforated and stretched and meconium came away." Ever since, there has been most obstinate constipation, for which she was treated privately and at hospitals with medicines and enemata with more or less effect; from time to time enormous masses of *fæces* were evacuated. Occasionally no *fæces* were passed for three weeks, but treatment was never delayed for a longer period than this. A diagnosis was not made.

When large masses passed, the child complained of pain at the anus. The stools were always hard and dry, of greenish or dark color, irregular in shape, remarkably free from odor. If treatment was withheld, absolute constipation resulted.

Urine.—Frequency of micturition was present, with great urgency if she was compelled to hold urine, as during school hours; the urine itself looked normal.

Until recent years no other symptoms existed, then intermittent swelling of the abdomen occurred, accompanied by colicky pains; also she lost control over flatus and any movement made her pass flatus, so that she was unable to stoop without this result, which worried her. She was becoming thinner and her appetite was small, but she had no headache, sickness, or other symptoms.

PHYSICAL EXAMINATION.—I was asked to see her by my colleague, Dr. W. Cecil Bosanquet.

Inspection.—The child was well nourished. The skin was clear. Tongue was clean. Mouth and teeth were healthy. Eyes were bright. She was rather pensive but mentally active and seemed a perfectly healthy child.

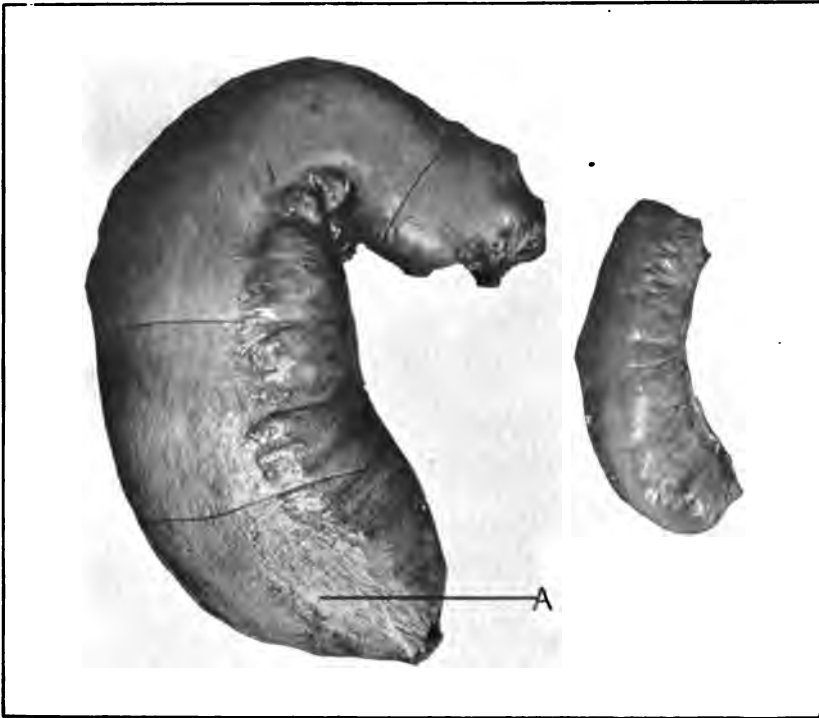
Abdomen.—This appeared normal in shape, possibly a little full below the umbilicus; movements on respiration were good; suddenly a marked arching of the recti occurred producing a phantom tumor extending from the pubis to the epigastrium, obviously due to the action of both rectus muscles, which felt hard and tense; it was accompanied by some discomfort—the colicky pains complained of—lasted about sixty seconds, and then subsided. Its onset was irregular in time. No other form of peristalsis was noted.

Palpation.—The abdominal muscles were relaxed except during the phantom swelling; but under the recti definite resistance was felt below the umbilicus; and above the pubis in the *right* hypogastric and iliac regions a hard, non-elastic mass was easily felt, indefinite in outline, the size of a tennis ball and slightly tender on deep pressure.

Percussion.—Over the tumor and some distance under the recti above pubis resonance was absent, elsewhere below umbilicus it was impaired; the flanks and epigastrium were resonant. Liver dulness was normal. Thoracic viscera were normal.

P. R.—The anus patulous, admitting finger easily and without spasm in least degree, but almost immediately, within 1 inch, its progress was impeded by what appeared to be a very hard, smooth, ovoid mass about 3 inches in diameter, which *seemed* to be situated *outside* the rectum in Douglas's pouch, the wall of the rectum

FIG. 1.



M. M., Case I.—The rectum and part of sigmoid as removed from M. M., also a portion of sigmoid from an older child distended by air for comparison. The greatly hypertrophied longitudinal muscle-fibres are well shown on the interior surface, especially at A.

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appearing to intervene between the finger and the mass. It was felt bimanually to be continuous with the mass above the pubis; it moved not at all. Further digital examination of the rectum was impossible, *fæces* were not palpable, and the rectum appeared obliterated by pressure between the (?) growth and sacrum.

The impression gained was most misleading, totally unlike the second case; and a diagnosis of possibly ovarian dermoid made.

The pelvic organs were not localized.

On admission to the Metropolitan Hospital, July 13, 1908, temperature was normal, and during her stay there before and after operation it remained so with a tendency to subnormal. Pulse 80; this varied from 70 to 90. Respiration was quiet and not frequent.

The physical signs were as above, but abdominal swelling was possibly a little more doughy. Resonance varied slightly from day to day. The *urine* was not examined for excess of indican but in every ordinary sense looked normal and was free from abnormal contents. Treatment of the bowel by purgatives and enemata was fruitless.

OPERATION.—C. E. July 18, 1908; under anæsthesia, no phantom swelling.

Through a median incision between pubis and umbilicus a large cyst-like structure appeared, median in position, its color somewhat like a simple ovarian cyst; on closer examination coarse longitudinal interlacing striæ were seen towards the right (see Fig. 1, *A*), afterwards found to be its anterior surface. The hand introduced found the mass extended deeply into the true pelvis and completely occupied the brim; above, it reached to near the left costal margin, and there formed a large inverted U, the limb towards the patient's left being much smaller and becoming continuous on the iliacus with the descending colon.

The small intestine occupied the right side of the abdomen and never presented in the wound.

On enlarging the incision the upper convex end was delivered and the pelvic structures were inspected: a small uterus and adnexa lay over the bladder, pushed forwards above the pubis; Douglas's pouch existed as a potential slit; the peritoneum forming the anterior wall lay tightly stretched across the front of the rectum as a band, concave upwards (see Figs. 11 and 12, Case II); into the

pouch the handle of a scalpel was passed. The mesentery of rectum and sigmoid was thin, in no sense hypertrophied, and except for the part attached to the highest part of the concavity of the Ω was *shorter* than usual. The veins were dilated and the inferior mesenteric artery was enlarged; the lymphatics were not prominent, and the lymph-glands were normal. No distention of the large bowel existed elsewhere.

The descending colon and the proximal part of the sigmoid were of normal size but abnormally mobile; the peritoneum being lax, it could be easily taken down to meet the lowest point where division of the rectum was possible (I am convinced it could be drawn through the anus). Doyen's intestinal clamps were put on the bowel and section of the gut was made about 2 inches along the proximal limb of the sigmoid; the mesentery was then divided as near the paries as possible, avoiding the trunks of the vessels; very few vessels were ligatured; the bowel was now attached below only. By insinuating the fingers into Douglas's pouch the peritoneum was stretched and the pelvic organs were packed forwards, the rectal contents were then "milked" from below upwards, and a Doyen's clamp placed below and a strong clamp above, and the rectum divided. Both ends were proved to have an abundant blood-supply and were united by a through-and-through catgut suture supplemented by Lembert's suture of silk. The lower end being so much larger in circumference was plicated to the necessary extent and the plications made permanent by vertical Lembert's sutures.

The abdomen was closed in layers and the patient put back to bed in excellent condition.

AFTER-TREATMENT, ETC.—Shock was practically unfelt; flatus passed same day; no distention, or sickness; slight pain in region of wound. For six days recovery was uneventful, being quite comfortable. Flatus was passed daily.

On the seventh day after operation (July 25) faeces passed naturally, without pain. Full diet was now ordered and a slight laxative, also a small rectal enema daily, and the subcuticular skin stitch removed. Her recovery was in every sense excellent.

Examination per rectum showed grip of the sphincters improved but weak still; rectum empty; no constriction, fold, or other form of abnormality detected, beyond slight increase of the ampulla

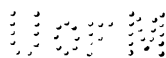
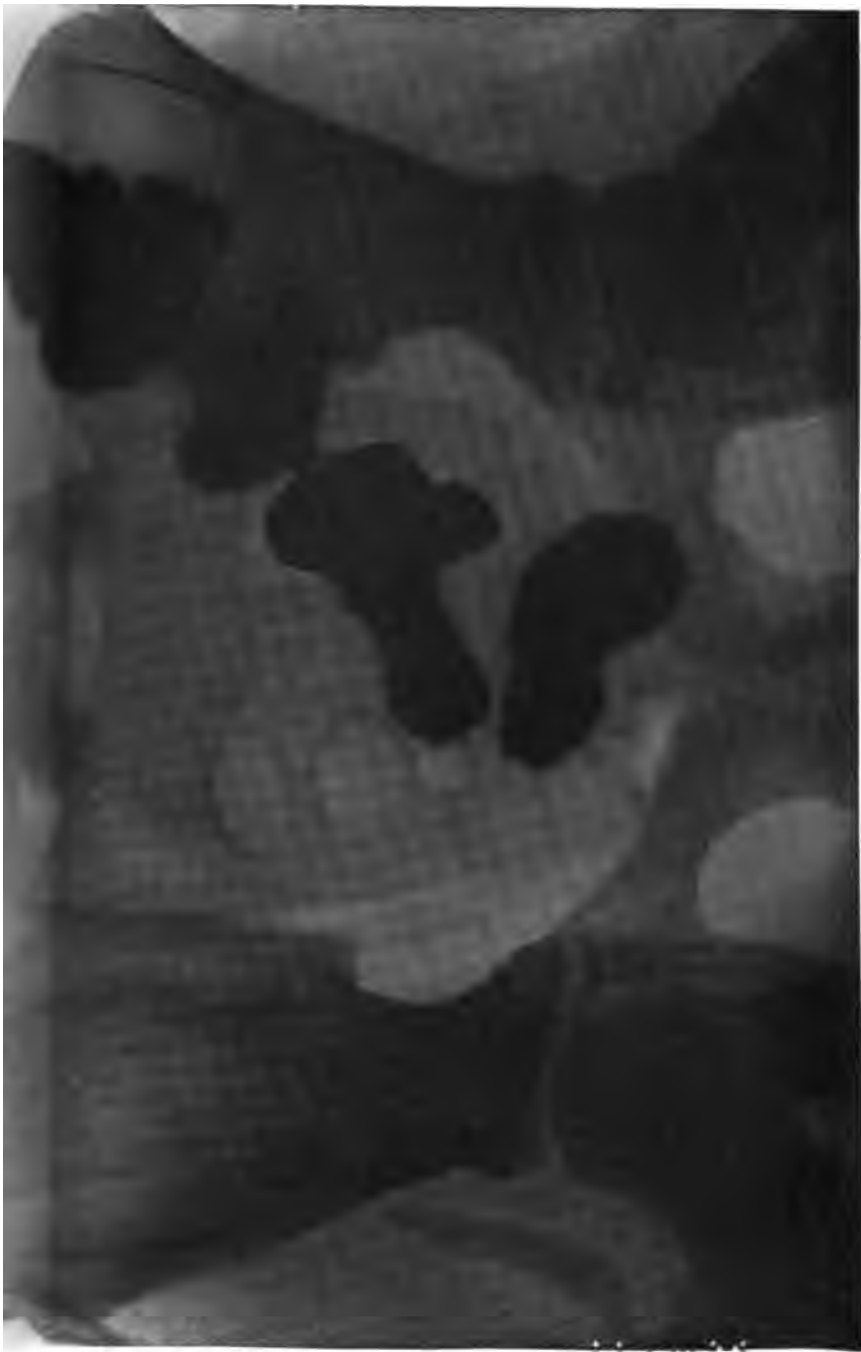


FIG. 2



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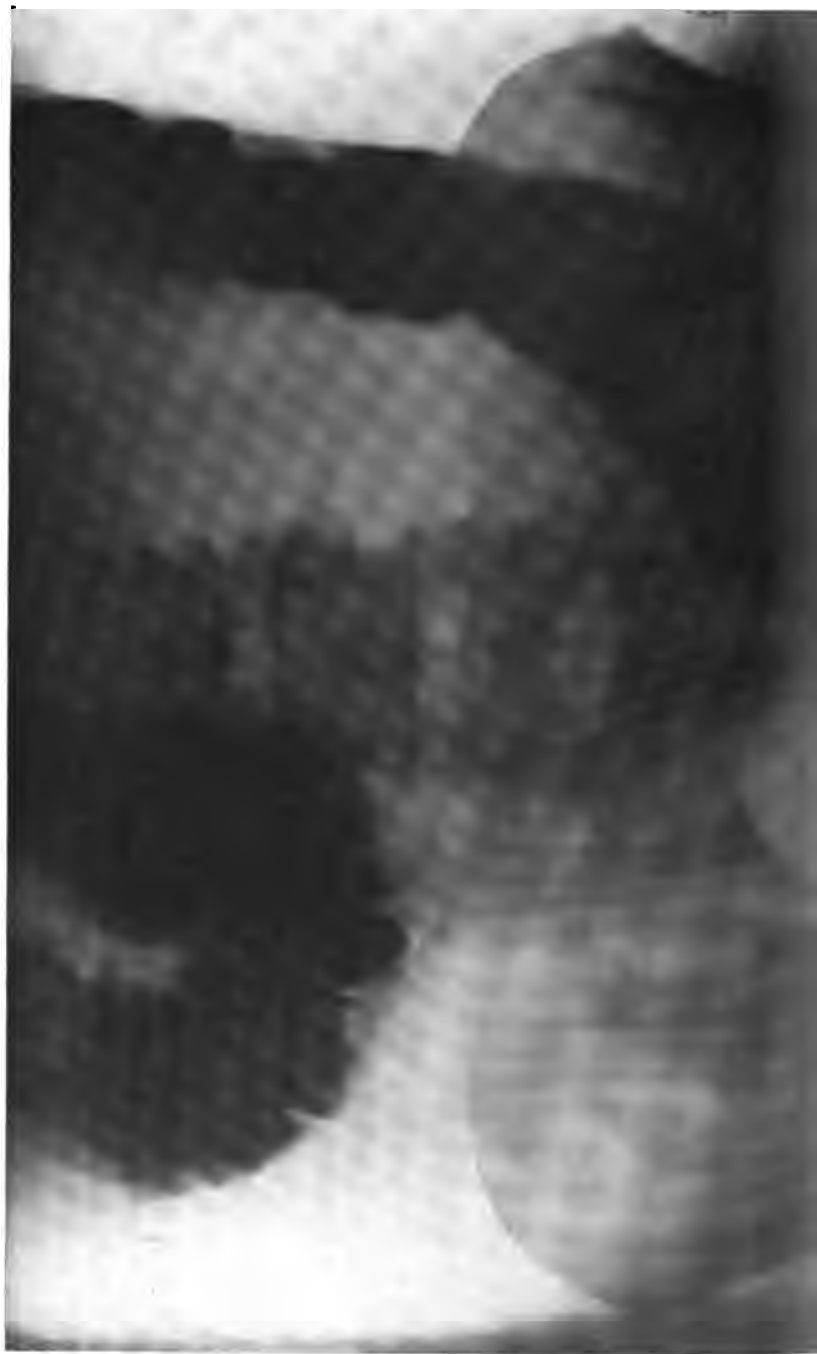
M. M. Case 1.—A skigram of the large intestine taken four months after excision of the dilated rectum and part of sigmoid. Carbonate of bismuth was administered by the mouth two days previously. The bismuth lightly spattered over the caecal mucosa enables its outline to be seen and shows a normal viscous.

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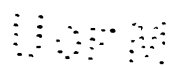
FIG. 3.



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M. M. Case 1.—Skiagram taken after injection of bismuth emulsion (6 oz.), catheter *in situ* in the rectum. Note the conical anal canal, the marked dip of the transverse colon, and the straight undilated condition of the portion of sigmoid and descending colon.
The rectum is distended to its utmost capacity, the point of anastomosis cannot with absolute certainty be made out; the constriction visible at junction of vertical and oblique portions on the middle of the sacrum is *not* the line of union, as I was able to convince myself through the screen when injecting the bismuth.



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FIG. 4.





M. M. Case I.--To direct attention to the S-shaped transverse colon, the left half of which, before operation (see Figs. 9 and 10), was pushed up by the dilated rectum and sigmoid, which had occupied the clear space embraced by the transverse colon above, the descending colon on the left, and the caecum on the right (see Fig. 2). The exaggerated loop as observed is an effect of the overgrowing by the dilated segments and clearly shows that in these cases of congenital dilation the "exaggerated loop formation" is not a cause of the condition but a result.

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anteriorly. She was kept recumbent, carefully dieted, and bowels attended to for three weeks; and on August 11, in the fourth week, she was discharged free from all symptoms.

November 6.—Readmitted for observation. Mother reported that bowels reacted to laxatives, but there was tendency to constipation if no medicine was given, which was easily relieved by a small enema. The child looked better, complexion healthy, and all symptoms had disappeared. Weight was four stone nine pounds.

P. R.—The ampulla of the rectum was exaggerated, forming a dilatation on the front of the bowel about 1 inch in diameter, where a small fecal mass lodged; if the finger were directed along the *posterior* wall it could be introduced vertically to its full extent.

EXAMINATION BY X-RAY by Dr. N. S. Finzi, physician to the electrical department of the hospital, November 16, 1908. Bismuth meals were given and an X-ray taken, but it was unsatisfactory.

On November 16 another photograph was taken (see Fig. 2), then a tube was passed into the rectum and bismuth emulsion 4 to 6 ounces was introduced and two photographs taken (see Figs. 3 and 4).

The introduction of the bismuth emulsion was watched through the screen and was interesting; at first the bismuth remained in the dilated portion, *i.e.*, slightly distending the lower 2 inches of the bowel, suddenly *without any peristaltic movements* it rapidly slid up the bowel until it reached the right hypochondrium—a proceeding resembling capillary action seemed to take place between the fecal contents and the bowel mucosa.

When the patient stood up a considerable quantity of the emulsion was passed per rectum. (*Note* the funnel shape of the anal canal indicated by streaks of bismuth about the catheter.)

January 9, 1909, six months after operation, I saw and examined the patient again. In every way the patient had improved. She had gained flesh and now could retain urine easily, urinating usually morning and evening. The mother had discontinued all treatment and reported that the bowels appeared to act variably once to three times a day; if the latter, patient passed small, irregular round masses on the second and third time and occasionally she passed a small round pellet when urinating.

P. R. Examination.—The sphincters offer definite resistance to

the finger but their tone was certainly defective and not normal for a patient of this age; she could produce a certain amount of grip voluntarily. The rectum contained fæces which were moist but firm and collected in the exaggerated ampulla (see note, Nov. 6); posteriorly the finger could be passed upwards into the bowel.

The mother was instructed to wash out the small mass twice a week, and I have no doubt if this is done the bowel will act once daily and no trouble will arise.

DESCRIPTION OF SPECIMEN.—The specimen with its contents was hardened by Kaiserling's method. As will be seen from Figs. 1 and 5, the rectum and sigmoid assume the shape of a distended stomach, the pyloric portion being formed by the ascending sigmoid limb, and the body and fundus by the rectum and descending sigmoid limb. Both ends appear to be blind, due to both having been tied and the specimen hardened while tied, otherwise they should be wide open.

The smaller figure is that of a sigmoid *distended* by air removed from the body of a child somewhat older than M. M. The three sharp lines are due to wire suspending the specimen. At A is best shown the interlacing hypertrophied longitudinal fibres, but these are seen almost everywhere towards the convexity, being best marked anteriorly and posteriorly.

Its dimensions are 20 inches (50 cm.) along the convexity; 13 inches (32.5 cm.) in circumference; 6 pounds 3 ounces in weight.

The bowel before removal is accurately represented by the skiagraph of the other case (see Figs. 9 and 10), as the two cases were identical in shape.

The *peritoneum* is opaque, smooth except where the muscle fibres stand out, and free from adhesions; there are no saculi or appendices epiploicæ. (At the operation the membrane had less lustre than usual.) It is hypertrophied.

On section the wall of the gut is hypertrophied generally, especially on the concave side, but here and there the thickening is only moderate, *i.e.*, slightly thicker than a normal bowel (for the proportion in the hypertrophy see microphotographs, Figs. 6 and 7).

The whole lumen was accurately filled with fæces of a bright

FIG. 5.



M. M. Case I.—The specimen opened: the lower is the empty half, the upper half contains the mass of feces which completely occupies its lumen—weight 6 lbs. The lower half shows folds of mucosa, best seen at A.

FIG. 6.



M. M. Case I.—Low power microphotograph showing a thin portion of the rectal wall, submucosa is partly detached. The relative proportion of the coats is obvious. The mucosa has been cut somewhat obliquely.

FIG. 7.



M. M. Case I.—A low power microphotograph of a hypertrophied portion of the rectal wall, the circular muscular coat is three times the thickness of the mucosa and longitudinal coat, which latter are about equal in thickness. All the constituent tissues are healthy.

FIG. 8.



M. M. Case I.—A high power microphotograph of the mucosa of a thin portion of the rectal wall, cut somewhat obliquely. It shows the Lieberkühn's crypts, goblet cells, and intercellular tissue normal and quite free from inflammatory products.

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green color which has been aptly described as resembling spinach (see Fig. 5). When the fecal mass was removed (Fig. 5, lower section), the mucosa generally was smooth, pigmented a brownish tinge; here and there whiter areas existed as though a pellicle had been removed; microscopically the brown pigmented portions consisted partly of altered mucus and amorphous *débris*.

Transverse ridges exist everywhere to some slight degree, but are most prominent at *A*, where, by analogy, the fundus and the body of the stomach would meet. No ulcers, erosions, or other sign of trauma or colitis are seen.

Microscopic Examination.—Except for the huge hypertrophy one might correctly describe the general appearance of the specimens as being normal in character (see Figs. 6 and 7).

Mucosa.—No evidence of necrosis of cells or intercellular tissue is noted, but the surface epithelium in the hypertrophied parts of the bowel varies; in some places it is almost normal, in others absent, and the crypts here open directly by dilated or shortened necks on to the surface; other places look as if the palisade of cells were blown down on its side, and every intervening stage is seen in a process of pressure atrophy.

In certain portions of the bowel there is seen on the free surface a layer of amorphous material, possibly surface epithelium, mucus, and *débris*; almost every cell in every crypt is a goblet cell (see Fig. 8). There is no evidence of fibrosis or inflammation, the *submucous tissue* is less than usual thickness, and the *muscularis mucosæ* is slightly hypertrophied. There are well-marked reduplications or folds of the mucosa and submucosa quite normal in appearance.

In the thinner areas the mucosa shows no other changes beyond the smaller depth of the crypts due to pressure atrophy and the almost total absence of surface epithelium. The *submucosa* is diminished, being thinner than in a normal colon.

The *circular muscular coat* forms three-fifths of the whole thickness of the wall, the longitudinal coat being one-fifth and the mucosa one-fifth; it appears normal in every respect, as does the longitudinal coat.

The *serous coat* is slightly thickened and there is some evidence of vascularity.

The hypertrophy in certain places is between three and four times that of normal bowel.

E. L., *ÆT.* TWELVE YEARS, MALE

FAMILY HISTORY.—Father, mother, and sister normal. There is a history of insanity on the part of one parent's family.

PREVIOUS ILLNESSES.—None except bowel trouble.

HISTORY.—Since birth there is history of obstinate constipation; then occasional attacks of so-called diarrhœa; and of recent years complete loss of control (incontinence) over his bowel, so that he soiled his trousers and bed constantly. "Liquid motion runs away from him day and night," and it was for this he was brought to the Gordon Hospital for Rectal Diseases. Previous to the onset of incontinence the constipation would last for weeks.

The incontinence is painless but defecation is painful, irregular masses coming away, often in very large quantity. Fæces are free from offensive odor and of a dark green or brown color. Appetite is good, never sick, occasional headache, and rarely has slight colicky pain in lower part of stomach before stool. *Urination* is frequent, every 3 to 4 hours, but he does not get up at night.

ON ADMISSION to the Metropolitan Hospital, July 24, 1908, temperature was 98.4°, and throughout it was never above normal, oftener subnormal. Pulse 80–90; respiration 24. Four teeth are carious, tongue is clear. Rather peculiar facies; the forehead is high, eyes somewhat sunken, bright, and intelligent; mouth pouting; face is somewhat flabby and puffed; mentally very alert; rather an introspective appearance.

ABDOMEN.—*Inspection.*—Movements on respiration visible in upper half, not below; no peristaltic waves or phantom swellings seen. Below umbilicus there is some fulness. Chest is well formed.

Palpation.—Everywhere except in the flanks a general sense of resistance is obtained on deep palpation—not muscular rigidity, but as though the abdomen in the central and lower regions contained a doughy mass; outside the semilunar lines a mass is easily felt extending to within 1 inch of the anterior superior spines, more definite on the *right* side, but the exact outline is indefinite; below, it extends into the pelvis, above it is lost about the level of the umbilicus. Slight tenderness is present over the mass.

Percussion.—Resonance is greatly impaired over whole mass, under right rectus above pubis dull.

P. R.—The anal canal does not exist as a tube, it seems to be merged in the dilated rectum and the sphincters are passive, some slight voluntary contraction is possible.

Immediately the finger is inserted it impinges on a hard dry mass of fæces, the periphery of which is just reached by the fingertip and its diameter is about 3 inches; the fæces are very hard and the mass is absolutely immovable; bimanually it is easily palpable but equally fixed. At the periphery moist fæces can be felt passing down over the mass, small pieces broken off are of a dark green color, free from odor.

PROGRESS.—Oil enemata at night, followed by soap and water in the morning, gradually brought away huge quantities of fæces, then laxatives were given and on the tenth day an *examination per rectum* was made: Sphincters were more active, no incontinence. The progress of the finger into the rectum was impeded by the vertical folds of mucous membrane which entangled the finger, but there was no real obstruction. Two inches above the orifice on the right posterior aspect was a large Houston's valve which appeared thicker than normal.

On August 9 patient was sent away for a holiday, rectum being empty.

Seen fourteen days later, in spite of purgatives I find *per rectum* that fæces were accumulating, and, as in the former case, this began in the front of the dilated rectum. He was washed out.

November 2, *i.e.*, in three months, he was readmitted with the history that in spite of treatment constipation gradually recurred but that incontinence had only reappeared three weeks before. The sphincters were again patulous and the mass was palpable as before but somewhat smaller. No excess of mucus was present.

The patient was fed on bismuth carbonate in bread and milk for three days, and my colleague, Dr. N. S. Finzi, skiagraphed the abdomen, but without a successful result. At Dr. Finzi's request he was then given charcoal to test the rate of progress of the food along the intestine. The charcoal was administered on November 4, on the 7th and 8th the bowel acted but no charcoal evacuated, on the 9th, *i.e.*, five days later, charcoal appeared.

November 16, patient was examined by Dr. Finzi and myself through the fluorescent screen, and X-rays taken. The first (see Fig. 9) showed minute traces of bismuth in the cæcum, and irregular masses incorporated in the fæces beyond the hepatic flexure; these opaque masses were due to the bismuth previously given by the mouth. A catheter was then passed into the rectum and an emulsion of bismuth gently injected and (Fig. 10) taken.

Most of the emulsion returned when the boy stood up. It was noticeable that when the photographs were being taken the boy could with difficulty hold his breath, whereas the girl, whose rectum and sigmoid had been removed, experienced no difficulty in holding her breath for the required time.

November 17, the patient was taken to the operating theatre in the best of spirits, as he was most anxious to have the operation; while being anæsthetized with chloroform (open method) his breathing stopped and the face became dusky, with marked circumoral pallor; heart was still beating. In spite of all efforts, however, he succumbed.

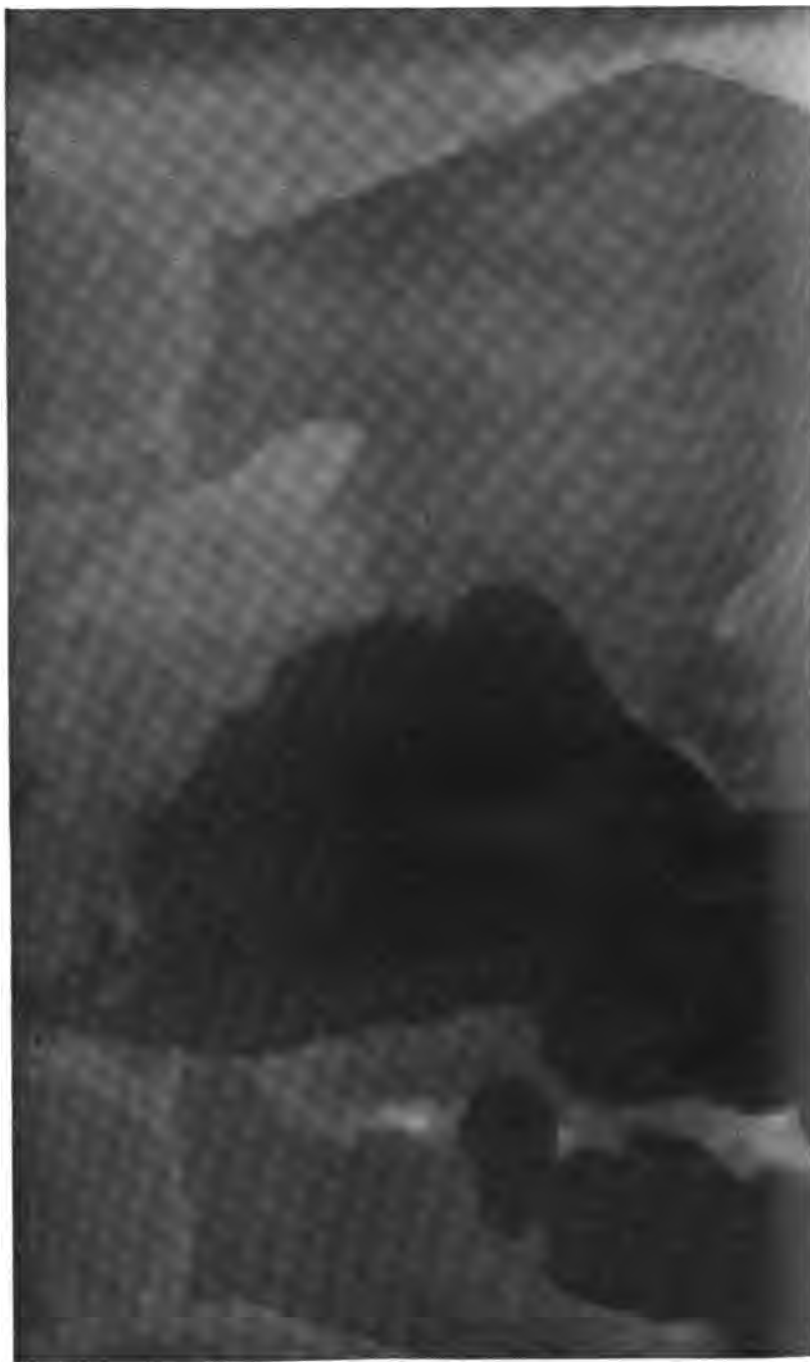
AUTOPSY.—The X-ray photographs of this and the former case show clearly the state of the rectum and distal limb of the sigmoid. The rectum so filled the pelvic brim that pressure on the ureters was being exerted and they were dilating, but no evidence of hydronephrosis existed. It was with very great difficulty and only after symphysiotomy that the hand could be passed into the true pelvis to remove the rectum and its mesentery with the firmly adherent bladder, along with the intact anus and perianal tissue. No changes existed in the mesentery; it was very short and thin, but the vessels were dilated somewhat.

The proximal limb of the sigmoid and the rest of the colon was normal in size and thickness. The transverse colon showed the peculiar shape exhibited in the skiagraphs, and the small intestine was packed to the right and somewhat under the dilated bowel.

The patient showed unequivocal signs of *status lymphaticus*, the thymus consisted of two well-marked lobes, the left being larger than the right; both together covered completely the palm of the hand. Numerous lymphatic glands were enlarged, a few in the mesosigmoid.

Description of Specimen.—The specimen shows that the greater

FIG. 9.





E. L. Case II.—A skiagram taken some days after bismuth meals were discontinued previous experiment with charcoal having proved that four or five days elapsed before the charcoal was passed per rectum. The small nodule in the left iliac fossa practically indicates the junction of the descending colon and the sigmoid.

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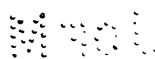
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FIG. 10.





E. 1. (See 11. A diagram taken immediately after Fig. 9, subsequent to the injection of bismuth emulsion, the catheter remaining *in situ*; the conical shape of the anal canal, indicating its patulous nature, is well shown. The rectum completely fills the pelvis (at postmortem compression of the ureters was found and the viscous appeared to have moulded itself to the shape of the pelvis and its brim).

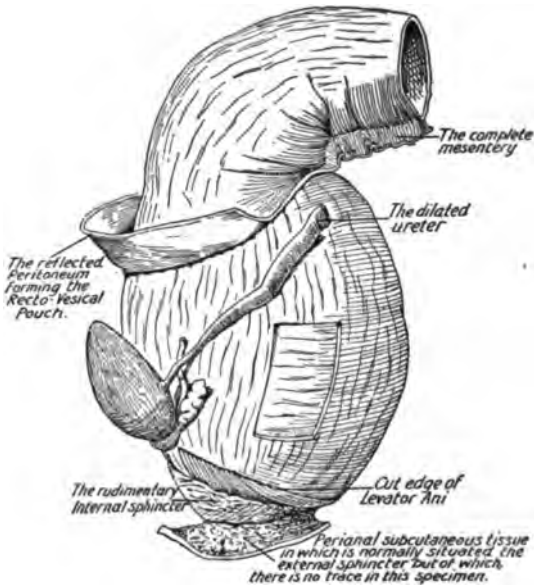


portion of the dilatation and hypertrophy is in the rectum (see Fig. 11).

The *vesiculæ seminales* and *vas deferens* were so compressed and adherent to the longitudinal coat of the rectum as to be with difficulty dissected free, while the bladder was distorted in shape.

The *internal sphincter ani* consists of a mass of muscle of a much lighter—grayer—color than the normal, its fibres are collected into interlacing bundles and not arranged in circular layers

FIG. 11



A slightly diagrammatic drawing of the mounted specimen of the rectum in the case of E. L. (Case II) in the R. C. Surgeons' Museum.

as usual, its depth is less than half a normal sphincter; there appears to be a considerable admixture of fibrous tissue with the muscle bundles. No doubt some of these changes are due to the abnormal shape of the anus, which, instead of being a canal about 1 inch in length, is a mere orifice opening immediately into the dilated rectum—much as, in labor, the cervix uteri merges into the body of the uterus. Thus the sphincter appears to grip the lower end of the much-dilated rectum, so that it does not form a complete sphincter but tails off gradually, and at the dorsal aspect no sphinc-

ter exists. Its color and admixture with fibrous tissue, however, and the arrangement of its muscle bundles are pathological. The *external sphincter* does not appear to exist, at least it is not visible to the naked eye in the dissection.

There is great hypertrophy of both muscular coats, greater in the circular. Internally there are no folds, valves, or other form of obstruction; the cavity generally is smooth, but a few mucosal plications exist here and there, especially at the site of Houston's valves; these are less obvious now than they were in life.

The specimen was not examined with the microscope.

PATHOLOGICAL ANATOMY

In order to avoid ambiguity it will be well to define clearly certain parts of the colon concerned in this affection.

The colon passing down the left side of the abdomen on to the iliacus has no mesentery, but at some point on the iliacus it acquires a mesentery and forms a large U-shaped loop having a proximal and a distal limb; the distal limb ends *where the mesentery ceases*, at the middle of the sacrum; this portion of bowel possessed of a mesentery is called the sigmoid.

The bowel which continues on from the middle of the sacrum to the internal orifice of the anal canal is the rectum and in adults is about three inches long; it has no mesentery. The peritoneum, which completely covers the sigmoid, covers only the front and lateral aspects of the rectum and is reflected from the front of the rectum forwards on to the bladder at the base of the trigonum, $1\frac{1}{4}$ – $1\frac{1}{2}$ inches above the base of the prostate, *i.e.*, 2 – $2\frac{1}{2}$ inches above the anal canal; the reflection of peritoneum marks off approximately the *position where the primitive gut joined the urogenital sinus*.

At this level *inside* the rectum is a prominent reduplication of the mucosa, the principal valve of Houston, situated on the right side and somewhat posteriorly; embryologically this marks off the rectum from the sigmoid.

The anal canal is a tube 1 inch long surrounded by the internal sphincter; its external orifice is guarded by a disc-like muscle, the external sphincter.

Congenital idiopathic dilatation in the vast majority of cases affects the sigmoid, which is dilated and its wall hypertrophied. If

FIG. 12.



E. L. Case II.—The whole large intestine from cæcum (on right) to perianal tissue (on left).

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the dilated sigmoid be traced downwards it *gradually* tapers into and becomes the rectum, much as the body of a hock bottle merges into the neck. This neck portion is not constant in length or calibre, but in some instances it is longer than normal and it is difficult to say where rectum begins and sigmoid ends; sometimes its wall is thicker than normal while its lumen is narrower than usual; in other cases the rectum is normal in thickness and calibre, while again it may be considerably dilated, *i.e.*, ballooned.

Probably some of the changes in the rectum are *secondary* effects of the dilatation and hypertrophy of the sigmoid, which lead to want of use of the rectum and also traction upon it, or to pressure from the overloaded sigmoid dropping into Douglas's pouch—all of which must be accorded due weight in considering the condition of the rectum. The exact cause of ballooning in these cases is unknown, and it may be that ballooning is normal to certain individuals; I have certainly found it present in otherwise healthy persons, and it therefore has no bearing upon the condition of the sigmoid; on the other hand, the ballooning may be an intermediate stage in the evolution of the disease as manifested in the two cases here recorded.

These two cases belong to a totally different phase of congenital dilatation and hypertrophy, inasmuch as the *primary site of the disease is the rectum*, which assumes an extreme degree of ballooning, *i.e.*, dilatation, beginning at the internal orifice of the anal canal and (possibly) involving the sigmoid secondarily, just as in the sigmoid variety the dilatation and hypertrophy may extend into the descending and transverse colon.

While, then, the anatomical *site* is different, I think the underlying defect which results in the dilatation and hypertrophy is of the same nature, namely, *an abnormality in the processes which take place at that stage of development during which the primitive colon ceases to open into the cloaca (urogenital sinus) and acquires its new opening at the proctodeum or perineal anus.*

On reviewing the literature recording cases of idiopathic dilatation of the large intestine—a duty rendered easy thanks to an excellent bibliography complete to January, 1908, appended to an exhaustive communication and report by Finney of Baltimore in *Surgery, Gynæcology, and Obstetrics* (British Edition), June,

1908, vol. vi, No. 6, p. 624—one is led at first to admit that they seem to fall into two groups as classified by Hirschsprung, viz.: (1) Those occurring in infancy, *i.e.*, true megacolon; (2) those occurring in adult life, *i.e.*, pseudomegacolon.

This impression, however, is greatly modified by a closer examination of the histories of some of the carefully recorded adult cases, and by bearing in mind the proverbial carelessness of many mothers concerning the health and habits of their children, and their consequent inability to give any useful information some years after the infancy of their children; one must also bear in mind the regrettable neglect of physical examination of the abdomen and bowel by physicians when cases of constipation come before them; thus, my two cases, although attended by practitioners and at hospitals more or less their whole lives, had remained undiagnosed until they were over twelve years of age.

When, in addition, one considers the prevalence of severe constipation and the rarity as a sequence thereof of the symptomatology associated with congenital dilatation and hypertrophy, and further that cases in which colitis has existed and been cured, especially ulcerative cases of the sigmoid, rarely develop the clinical picture of idiopathic dilatation but tend finally to atrophy and contraction rather than dilatation and hypertrophy—in view of these facts one is still further disinclined to accept this classification, and to believe, on the contrary, that most of these peculiar cases are congenital in origin—true megacolon—modified by, rather than produced by colitis and coprostasis.

In the adult cases it is impossible to avoid the obvious criticism that *degrees* of the disease may exist, and that the cases which have lived to adult life were the subjects of a mild variety of the affection which became aggravated in the course of time.

In support of this contention is the well-known fact that periods of quiescence and improvement *do* occur in undoubted cases of congenital idiopathic dilatation.

I am convinced a pseudomegacolon, *i.e.*, a truly acquired condition, also exists; and in this connection I cannot refrain from expressing the opinion that its origin will be elucidated when the pathology of ileus becomes clearer.

I think the classification, in view of the large number of cases

recorded since Hirschsprung's last communication in 1888 and the information derived therefrom, should be modified thus: (1) True megacolon (congenital dilatation and hypertrophy), infantile and adult; (2) pseudomegacolon, in adults.

With regard to the two cases herein recorded there is no doubt as to the congenital origin. One, the female, had an imperforate anus and the constipation dates from birth; the other, E. L., similarly had constipation from birth and at his death was found to be the subject of status lymphaticus, an affection in all probability due to some congenital defect of development. In his family also is a history of insanity, which I mention here because a large number of pseudomegacolon cases occur in lunatics; *had this boy lived and become a lunatic* the association of dilatation and hypertrophy with the mental condition might easily have arisen.

DIAGNOSIS

The diagnosis of the condition of idiopathic dilatation and hypertrophy should not be difficult in the majority of cases when well developed; but there is difficulty in recognizing the disease while the subjects are very young and the stage of dilatation is not extreme, more especially in the type of disease which involves the rectum.

The importance of early diagnosis in view of treatment is extreme, as it is during an early stage that measures of a radical nature can be best carried out, as I am convinced that the *degree* of dilatation and hypertrophy *increases progressively after birth*.

That dilatation and hypertrophy exist during intra-uterine life there is abundant evidence to prove, and Keith² states that in all the cases of malformation of the rectum and anus examined by him both are always present; but the tremendous stages to which it attains in infancy are consecutive to obstruction and stagnation of the bowel contents.

I think that every case of *severe* constipation in infants, dating from birth, should be considered sufficiently grave to merit thorough investigation as an incipient case of congenital dilatation and so to regard it until disproved by the result of medical treatment.

The real value of sigmoidoscopy in diagnosis I was not able to test, but I doubt whether it is sufficient alone, in an early case, to

enable one to express a definite opinion that a case is one of congenital dilatation.

SYMPTOMS.—In an early case these consist in:

1. *Severe constipation from birth*, the passage of the meconium even being delayed. Some records state that the onset of constipation was delayed weeks or even months, but I take these statements to indicate want of observation and thought, as probably 90 per cent. of the cases were constipated from birth; the fact that a few days elapse before the constipation is manifest is what one would expect and would constitute "constipation from birth."

The constipation is such that the result of even severe treatment is unsatisfactory; purgatives, enemata, massage, etc., afford only partial relief, the condition returning on the cessation of treatment; and absolute constipation may result for weeks or months without apparent discomfort or ill-health until treatment is again resorted to.

2. *The Character of the Stools.*—The fæces passed are always dry, usually ill-formed masses not assuming the shape of the sigmoid, markedly inoffensive in odor and of a greenish color. In very young infants the fæces may be pultaceous with admixture of solids.

The quantity passed as the result of vigorous treatment may at times be very great, the mere quantity suggesting a large colon.

3. *The absence of symptoms*, both local in the abdomen and general as affecting the health—indeed the patient may seem quite healthy; not infrequently there may be slight colic, and pain at the anus during defecation.

4. *Abdominal distention*, in the sigmoid variety of the disease, early becomes apparent and at first is variable but soon becomes constant, most marked at first in the left half of the abdomen in the iliac and umbilical regions, but rapidly increasing and involving a greater area of the abdomen. Sluggish, unwieldy peristaltic movements may be apparent. The abdominal muscles are flaccid. The swelling is generally resonant and with the stethoscope one should occasionally hear succussion sounds and borborygmi; under the severest treatment it is almost impossible to remove the whole abdominal swelling. If a large-calibre tube be passed 5 to 6 inches *after treatment*, some fæces may still be evacuated, if liquid, or may be washed out if solid, indicating an imperfectly emptied reservoir. There is no obstruction to the passage of flatus.

5. *Examination per rectum* generally elicits the fact that the rectum is empty (*i.e.*, in the sigmoid variety of the affection).

Occasionally the distended sigmoid may be felt through the anterior wall of the rectum, or the latter may be ballooned or constricted.

6. *Radioscopy after bismuth injections, and sigmoidoscopy*, will in future help in the diagnosis.

The *later symptoms* which are recorded by various observers as primary symptoms of the disease are usually due to *colitis*, and often overshadow the earlier symptoms, but nevertheless should only be apportioned their proper place in the clinical picture.

They consist in irregular diarrhœa, which, however, never empties the colon; solid fœces may still be evacuated by a long tube after such an attack; the character of the stools now alters, tending to become more liquid and pultaceous, though solid masses will always be passed from time to time, and an offensive odor develops; while the abdominal swelling increases and the general health begins to suffer.

Although these children appear to be in good health they are not robust and gradually tend to emaciate; they have periods of quiescence succeeded by exacerbations of symptoms, with increase of distention and some ill health. Any intercurrent affection rapidly develops and not infrequently they are carried off in a few days by chest complications, or they suddenly develop copræmic or uræmic coma and die.

When the disease affects the rectum primarily, as in the two cases here recorded, the symptoms as learned from these during the first eight years may be taken as typical, and consist, as before stated, of: (1) The typical constipation. (2) The invariable presence of hard, dry, dark-green masses of fœces, passed with great difficulty and some pain. (3) *No obvious abdominal distention*, but careful examination will elicit some abnormality in the hypogastrium, especially on the *right* side of the midline. Occasionally peristalsis or phantom tumor is seen. (4) By repeated *examination per rectum* the enormous mass of fœces should be palpable and at once betray the condition. However, as in the case of M. M., it may be impossible to *feel* the fecal mass, though one examination should not suffice; if possible an examination under anæsthesia

should be carried out, when it is almost certain that the fecal mass may be felt digitally and bimanually, rendering the diagnosis certain. (5) Bismuth injections and radioscopy will decide the question.

As before stated I think all other symptoms are superadded as a result of infection of the bowel—colitis—or from malnutrition and the mechanical disabilities.

DIFFERENTIAL DIAGNOSIS.—This will depend upon (a) the *history*, especially that of infancy and childhood; (b) the clinical picture; (c) thorough examination.

Intestinal destruction, dysenteric and septic mucosal infections, tuberculous peritonitis, cancer of the bowel, and pressure on the rectum have many local and general signs and symptoms which should differentiate them. The presence of mucus and blood in the stools, ascites, vomiting of a special type, and the general condition should lead one to suspect some other lesion than congenital dilatation. Indeed I think the diagnosis would be missed chiefly in the case of any one to whom the condition of congenital dilatation was unknown or unfamiliar.

The differential diagnosis of acquired megacolon of adults, also chronic volvulus, from congenital dilatation would be more difficult, but should be possible if the history from infancy is complete, as *the complete clinical picture of congenital dilatation is unique.*

That boys are affected three and a half times more frequently than girls, and two men are affected to one woman, may help in the diagnosis.

In many of the recorded cases the picture has become confused by the sequelæ of the disease; but the early signs and symptoms should be sufficient to lead to the correct diagnosis.

PROGNOSIS

The prognosis and course are always grave: some infants die within a few months of birth; others live to adult life, having periods of improvement from time to time, but nearly always followed by exacerbations, each graver than the former.

Owing to malnutrition, worry and mechanical inconvenience, patients do not thrive and are less resistant to intercurrent disease; but it appears to me that the most important element in prognosis

depends upon the ability to avert the onset of colitis by careful attention to the condition of the oral cavity and the nasal chambers above, and upon sterility in using rectal enemata. In the case of rectal congenital dilatation there is great probability of ureteral pressure at the pelvic brim, especially in males, leading to disorganization of the kidneys, thus interfering grossly with the two great *eliminative systems*. A large proportion of the cases recorded had definite hydronephrosis, which indicates the importance of this danger. One of my cases, the male, had obvious ureteral pressure.

The result of medical treatment must necessarily be finally unsatisfactory. A degree of relief and comfort may be afforded these patients by rectal manipulations and by medicines, and the abdominal distention may be kept under, *but only for a time*; and this is gained by devoting close and constant attention to the patient, which necessitates an invalid's existence, cutting off the children from a normal existence, especially when they attain to school age and adolescence. Prognosis must therefore be influenced by the transference of cases to *surgical procedures at an early age*, when I think the outlook quite good.

Finney says "the younger the patients the worse the prognosis." Surely this simply means that in the particular patients who have lived to an older age the disease has been initially less grave.

TREATMENT

From what has preceded it follows that the treatment must be surgical, and in my opinion the best course to adopt is that of excision with an end-to-end anastomosis. All the best results have followed this operation; the only question to my mind depends upon the details to be followed out in carrying through the operation and the time when it should be performed.

If the patient is quite an infant when the condition is diagnosed and facilities and means exist to devote great care to the child, I believe by systematic medical treatment the dilatation can be kept within moderate bounds and the child's nutrition will suffer little or not at all until it is about three years old, when excision and anastomosis can be carried out at one stage.

If, however, these ideal conditions do not hold, rickets and malnutrition supervene, the dilatation goes on apace, and any severe

operation would prove fatal. In these cases, which necessarily are hospital cases, a reasonable period should be devoted to rigid medicinal treatment and careful feeding while the child is kept in bed; massage to the body generally, as well as to the abdomen, should be carried out, and the condition of the infant improved as much as possible.

Fermentation and decomposition of the contents of the colon will be modified if not prevented by petroleum emulsion.

Then, when a definite period of quiescence exists, and the colon is practically empty, an anastomosis between the healthy gut above and below should be carried out.

The exact form the anastomosis should take is debatable, in most instances it has been a lateral anastomosis excluding the loop of dilated sigmoid; but I venture to think the better plan would be to sever the gut above, invert and oversew the cut upper end of the dilated bowel, and implant the healthy bowel end into the *constricted* portion of the rectum, *below* the narrowing neck of the dilated sigmoid. This can be done as quickly if not quicker than lateral anastomosis.

The loop now has no communication above but empties its secreted contents into the rectum below.

Medical measures should still be rigorously carried out, and in two or three months the loop should be excised.

If the condition of the child is good and warrants it, the loop may be excised at the primary operation, as however enlarged the bowel may be, it is the extent of mesentery which has to be dealt with which is important, and in these cases the mesentery is *usually not larger* than normal.

Objection will be raised that *lateral* anastomosis has been carried out, the sigmoid excised, and *new loops have formed involving hitherto unaffected bowel*. I think that, had strict medical treatment been persisted in, these cases would have shown better results, at least big loop formation ought not to arise. I also think the type of anastomosis to be chiefly responsible, as I find it is never as satisfactory as end-to-side or end-to-end union. I will refer to complete excision of sigmoid, rectum, and anal canal later.

In regard to the type of case similar to the subjects of this

communication, in which the true rectum (right down to the anal canal) is the seat of disease I feel that the result in M. M.'s case justifies me in advocating similar steps. After a personal experience of thirty excisions of the rectum and four of the anal canal for cancer—twenty of the rectal cases having been perineal operations in which the mucosa of the anal canal has been dissected off (Whitehead's operation), and the *sole damage* to the sphincters has been that they were split posteriorly and the sigmoid then brought down and sutured to the perianal skin—I have come to the conclusion that even with primary union it is almost impossible to carry out these steps and obtain a true and sphincteric action of real value. Also, in these cases the weak expulsive power of the sigmoid is such that normal defecation cannot be carried out, portions of stool are retained in the colon; and a collection gradually results which is expelled from time to time either naturally, by a form of diarrhœa, or by the aid of purgatives; so that the best *functional results* are obtained by keeping the patient definitely constipated and producing a stool by periodical laxatives, every second or third day, and this desirable result can *only* be obtained when the bowel is *absolutely free from colitis*.

If there is the slightest colitis this is impossible in spite of medicines, and the patients are constantly passing liquid fæces, in fact are in an unpleasant plight. I find that in the presence of oral sepsis, therefore, good functional results after excision of rectum, or in colostomy, are impossible, for these patients have constant frequency—"diarrhœa"—and are miserable.

The lessons thus learned have impressed me with the great desirability of never interfering with the anal sphincters, certainly not the internal sphincter, if it can possibly be avoided.

In cancer cases the absolute necessity of splitting the sphincters posteriorly to afford facilities for removing the mesorectum and for drainage can be overcome—certainly in women, by a transverse perineal incision between rectum and vagina, stripping these organs apart and operating from the front, and if the growth is sufficiently high above the sphincters the lower inch or so of rectum can be retained, the sigmoid and rectum can be invaginated by Maunsell's method through the dilated uninjured anus, and an end-to-end anastomosis carried out, all of which steps I have successfully

carried out and which therefore can be the more safely carried out in these non-malignant cases. For the foregoing reasons I would not advise the operation carried out by Treeves¹⁰ and others for the sigmoid variety of the disease, in which they have excised the anal canal as well as the rectum and sigmoid. I am convinced these patients' histories, if carefully inquired into, would exactly correspond to that of the cancer cases, namely, an irritating condition of constant desire and effort at defecation and washing up.

In the rectal dilatations resembling my two cases I would therefore advise a laparotomy with an end-to-end anastomosis, excising the rectum as low down as possible, the dilated lower portion being pleated vertically, while the ampulla, which will remain, should be washed out every other day or so, a proceeding very easily carried out and which will entirely prevent future trouble, *while leaving the patient absolute control over the function of defecation.*

To make clear my point in the treatment of congenital dilatation of the rectum, I will repeat that interference with the sphincters such as is carried out in excision of the rectum for cancer entails such loss of control, not only of *retention* of 'fæces but of *expulsion* also, that the existence of such patients is henceforth largely occupied in attending to the pseudodiarrhœa that results; whereas if an end-to-end anastomosis is carried out *leaving a portion of the dilated rectum and the sphincters intact*, their condition is infinitely more comfortable and entails much less attention on their part, at most the administration of an enema daily or on alternate days, while they possess absolute control of retention.

ETIOLOGY AND PATHOLOGY

Assuming the congenital nature of the defect, yet when the many views as to causation are studied in conjunction with the pathological reports it is perfectly clear that although the *majority* of the cases may have a common, *i.e.*, single, underlying factor, it is impossible to conceive a single defect that would explain the *details* of the varying pictures presented by the developed disease, unless most of these details *are grafted on* to the primary defect after birth.

The theories advanced may be summarized thus:

1. ANATOMICAL CAUSATION.—Two explanations of the conditions may be included under this head.

a. *An abnormally long mesentery* with tendency to torsion. But the vast majority of the cases controvert this statement, my own two among them, inasmuch as the mesentery was shorter than usual. Finney says, "Indeed in but comparatively few cases is the mesentery found by actual measurement to be unusually long." The increased length of the mesentery may with justice be considered a *result* rather than a cause of the condition.

b. *Increased length of the colon with multiplication and exaggeration of its loops*, especially the sigmoid, the dilatation and hypertrophy being secondary to and consequent on accumulated gas and fæces.

An examination of Figs. 3, 4, and 9 shows in *both* my cases a multiplication and exaggeration of the loop of the transverse colon which has assumed an S shape, but in these cases this is purely a result of the monopoly of the left half of the abdomen by the distended rectum and sigmoid—a matter of accommodation—as otherwise the transverse colons in both cases were normal. That increased length of the loops may be purely acquired is proved by the record of cases reported on after operation.

Also I have a case of pseudomegacolon (truly acquired) under my care in whom the transverse colon forms a loop descending into the false pelvis, but whose symptoms entirely disappear under suitable laxatives.

2. MECHANICAL CAUSATION.—Five theories may be mentioned.

a. By *spasm* of the sphincter ani, with and without fissures, and of other segments of the colon. With regard to spasm of the sphincter ani I have operated on over ninety cases of fissuræ in ano, the most potent cause of spasm, six of whom were under sixteen, and examined children with spasm of the sphincters from other causes, but in no case have I ever observed symptoms and signs at all suggestive of idiopathic dilatation.

I fail to see why spasm of the anal canal should produce *sigmoid* dilatation and hypertrophy even were it capable of leading to *rectal* dilatation and hypertrophy; the sigmoid alone should not be involved.

Cases of enterospasm have been operated upon and the con-

tracted bowel digitally and visually examined, but in no cases have I seen or read of symptoms and signs similar to the disease under review. I regard spasm of any part of the intestine as a manifestation of local irritation of the mucosa by mechanical or bacterial irritants—enteritis and colitis—and quite inefficient to lead to dilatation and hypertrophy.

My own two cases which suffered from *rectal* dilatation and hypertrophy had *patulous* sphincters, and the dissected specimen of E. L.'s case shows apparent *absence* of the external sphincter and aplasia (congenital deficiency) of the internal sphincter; and spasm cannot possibly have existed in either patient.

b. Obstruction by folds of mucosa, i.e., valve formation and other unknown obstructions, possibly of a functional character. Simple folds of mucosa have been demonstrated at operation and postmortem in certain cases, and to their presence has been attributed the dilatation and hypertrophy (Perthes³); it seems rather difficult to accept this explanation of obstruction, in a tube of the calibre of the large intestine, by a fold, in no case more than *partially* encircling the bowel and of comparatively little depth.

Yet I know from experience that a small membranous transverse stricture following an operation for hemorrhoids, involving only the dorsal aspect of the canal at the junction of anus and rectum, *will* produce marked constipation, possibly acting less as a mechanical obstruction *per se* than by interfering with the relaxation and normal function of the internal sphincter.

In the case of M. M., when first seen and examined by Dr. Bosanquet and myself, tissue was found to intervene between the mass of faeces and the finger; what this was I cannot say beyond that it must have been due to distortion of the anal canal, which was, as it were, intussuscepted into the rectum and produced a condition analogous to a retroprostatic pouch in the bladder, but this disappeared when the rectum was quite empty. In the case of E. L. a Houston's valve of unusual size was detected 2 inches or so up on the right posterior aspect, whereas accumulation of faeces first began anteriorly in the ampulla of the rectum; *it is possible that the valve directed the faeces anteriorly, which thus missed the anal orifice*, and the expulsive force of the bowel was expended in driving the fecal contents against the perineum; were the disease found

above the valve instead of being equally marked below it, one might have considered the rôle of the valve to be of greater importance.

Nevertheless in the vast proportion of cases no valve fold or other obvious obstruction has been demonstrated. In neither of my cases could I find, clinically or by examination of the specimen after removal, any fold, valve, or kink which, by any stretch of the imagination, could be interpreted as the true cause of the disease.

c. Pressure exerted on the rectum by pelvic tumors, perirectal and pericolic adhesions, etc.

d. Defective expulsive power by separation, etc., of the recti, atony of the bowel, and general weakness. In neither of my cases were any of these factors present; besides, the marked hypertrophy of the muscular coats of the bowel renders these views untenable and these cases probably belong to the pseudomegacolons alone.

e. As the result of *colitis*, in which from decomposition of the faeces gas accumulates and produces dilatation, peristalsis is rendered more difficult and hypertrophy results. These should not be classed as primary causes but as modifying factors only.

I think the foregoing theories may be quite safely put aside as unsatisfactory and insufficient to explain the condition, and those which follow are really identical in that they are founded upon the basis of a congenital defect. Hirschsprung⁴ simply states this fact, implying that the whole thing, dilatation and hypertrophy, is the defect; and Concetti⁵ contents himself with attributing the defect to aplasia (*i.e.*, imperfect development of the *musculature*) of the rectum, the rest being secondary thereto. Others make out the defect as one of the nervous system, and one of the most recent of these writers, Hawkins,⁶ considers the condition to be best explained as a neuropathic dilatation and hypertrophy; while Finney's¹ case by analogy and with every justice is considered an example of gigantism.

Personally I think all these opinions to be but partial truths, and that the dilatation and hypertrophy, while present in some degree from birth, *i.e.*, intra-uterine in time and consequently congenital, are consecutive to and dependent upon a *preceding* (earlier) defect of the bowel beyond, *i.e.*, they are mechanical in nature, the true disease being imperfect evolution or retardation of the hindgut (rectum) or anus, consequent in all probability on chorionic disease

(inflammation or degeneration?). The mystery therefore is the nature of the chorionic disease and its exact effect upon the structure and functional activity of the hindgut.

Keith² in his paper states that hypertrophy and dilatation is found in all cases of imperfect development of the rectum and anus, ante- and post-natal.

3. GIGANTISM. HYPERNUTRITION.—Finney's case presented marked hypertrophy in the vascular and lymphatic structures in the mesentery (lymphangiectasis) exactly corresponding in site to the dilated and thickened colon; and the submucosa of the colon itself, with the lymphatic and vascular constituents, was similarly affected. The *submucosa*, the circular muscular coat, and the longitudinal, were almost equally hypertrophied, while the mucosa was little thicker than the normal but greatly infiltrated by cellular elements, the hypertrophy thus affecting the bowel wall more uniformly than in the majority of specimens. He therefore regarded his case as analogous to macroglossia and macrocheilia.

The epithelium of Lieberkühn's crypts showed few goblet cells. In my two cases the picture is quite unlike this; the submucosa is as thin as in a normal bowel and of the same degree of vascularity, the circular muscular coat is three times thicker than the longitudinal coat, which is about equal in depth to the mucosa. The epithelium in Lieberkühn's crypts was almost all goblet cells, and in the case of M. M. there was absolutely no evidence of inflammation or fibrosis.

4. APLASIA, *i.e.*, incomplete or imperfect development of the *musculature* of a segment of the colon.

5. A CONGENITAL NERVOUS DEFECT DESIGNATED BY HAWKINS BY THE NAME OF NEUROPATHIC DILATATION AND HYPERTROPHY.—The aplasia is usually situated just above, or at, the junction of the sigmoid and rectum, and if it exists it interposes a physiological block in the course of the bowel, and effective continuity in the vermicular expulsive movements of the colon ceases here. As a result, Concetti,⁵ who promulgates this view based on a carefully examined specimen, attributes the dilatation to accumulation of gases (due to fermentation of the intestinal contents), followed by accumulation of *fæces*, which results in hypertrophy of the colon as a result

of increased work above the block. He attributes some of the hypertrophy to fibrosis from toxic infection.

I think this explanation of aplasia in a broader sense than defective musculature to hold true of most cases, if not all, of the sigmoid variety; several of the operated cases referred to by Hawkins and others afford positive proof that the dilatation and hypertrophy is a secondary process and that the lesion, whether nervous or what not, must be strictly limited to the rectum.

Thus in Case VIII in Hawkins's ⁶ series, a lateral anastomosis was made between the unaffected colon above the loop and the unaffected portion of the sigmoid below the loop, which was thus short-circuited; necessarily a small portion of sigmoid, *apparently healthy and undilated*, existed between the rectum below and the anastomosis above.

As the short-circuited loop tended to become volvulosed it was excised at a second operation, thus "the patient was provided with a short, fairly straight passage from iliac colon to rectum without any lateral *cul-de-sac*."

At a third operation rendered necessary, it was found that the small portion of hitherto *unaffected sigmoid* intervening between the rectum and the anastomosis had "dilated into a loop nearly as large as the original loop."

A similar experience is related by Richardson,⁷ who states that the "line of suture forming the lateral anastomosis was situated in the centre of a *new* loop which formed, and which involved what was previously unaffected bowel *below* the original loop and normal descending colon *above* the original loop."

Assuming aplasia then in these and similar cases, the physiological block must have existed in the *rectum or anus*, yet why is the dilatation so gradual and why after the anastomoses should the hitherto undilated neck become so dilated and hypertrophied, the conditions below, in the rectum and anus, remaining as before operation?

If the primary defect be nervous in nature, the nerve lesion must be very strictly limited to one small segment of the bowel, although it involves both splanchnic and somatic elements and although it manifests itself in some cases as of a paralytic nature and in others of a spastic condition. These cases, whatever else

they may suggest, *prove* that the dilatation and hypertrophy may be entirely acquired and need not be congenital, even in point of view of time alone, irrespective of development.

6. HIRSCHSPRUNG⁴ looked upon the whole condition as a primary antenatal process, either an anomaly of development or due to some unknown pathological factor.

In so far as the dilatation and hypertrophy are concerned I cannot agree with this; they are merely effects, not primary defects; but otherwise his statement is irrefutable, although it does not carry one nearer a solution of the actual defect.

My own two cases appear to be *anatomically and clinically* identical, with a few additional points in each case. Thus the girl suffered also from imperforate anus and showed a phantom tumor, while the boy was proved to be the subject of status lymphaticus (its exact relationship remains to be proved) and during his later years had incontinence of *fæces*.

The presence of the imperforate anus need not necessarily have any causal bearing on the dilatation and hypertrophy, as it was absent in the boy; nor need the fact that the boy had incontinence of *fæces* weigh with us, as I have shown that this is a later symptom engrafted on to the primary constipation and due to colitis, probably acquired from a definite degree of oral sepsis.

In view of Finney's¹ case of lymphatic gigantism the presence of status lymphaticus in this boy, a condition affecting the lymphatic system and possibly a congenital disease, without any lymphatic abnormality in connection with the rectum is interesting.

The condition of phantom tumor has often been recorded in these cases; personally I think they are always partly voluntary in nature and of no moment in pathogenesis.

Some pertinent enquiries require solution:

The fact that in the vast number of cases of congenital dilatation and hypertrophy the sigmoid is the dilated portion leads one naturally to enquire whether there is not some more complicated developmental factor associated with this portion of the bowel than exists in the remainder of the *primitive colon, which terminates at the sigmoid, not at the anus*; it may be such a simple matter as the presence of an imperfect sphincter at the junction of the sigmoid and rectum, as suggested by Cantlie.⁶

The fact that *normally* it is the sigmoid which acts as the reservoir for the faeces, while the rectum is empty, demands some such explanation, which is not an improbable one seeing that the primitive colon ends at the sigmoid (Wood Jones⁹) and here joins the urogenital sinus by an opening which possesses a sphincter (Keith,² see below).

When, in addition, we find recorded amongst these cases of congenital dilatation and hypertrophy instances of definite hypertrophy of the lower part of the sigmoid, and other cases of similar hypertrophy without dilatation above, one cannot dismiss Cantlie's suggestion without serious consideration and disproof.

This disease therefore may be simply due to an exaggerated action of a persistent sigmoid sphincter; and although I know of no developmental evidence to support this view according to modern interpretation of *human* embryology, I think *comparative* embryology does afford evidence to support such a sphincter action at *this anatomical site*.

Turning to the question of the small minority of cases of congenital dilatation and hypertrophy when it affects the rectum proper, among which are the two cases now placed on record, some other factor than a persistent sigmoid sphincter is necessary to explain the condition; and this in my view is associated with the formation of the *cul-de-sac* which eventually forms the adult rectum, and which according to Wood Jones is a prolongation backwards of the primitive colon, *beyond its cloacal anus at the level of the trigonum of the bladder*.

I feel convinced the true explanation of these cases will be elucidated solely by careful study of (1) comparative embryology of the evolution of the colon and rectum; and (2) of antenatal pathology. As suggested by Keith,² the importance of the latter is shown by the fact that it is almost certain that nearly all, if not all congenital defects of the *limbs* are due to *pathological* processes affecting the chorion; and it is therefore not improbable that many other developmental errors, amongst them this peculiar affection, may be initiated by pathological conditions affecting the embryo.

By a study of the evolution of the hind end of the gut *confined to the human embryo*, and an examination of certain pathological specimens of malformations of the rectum, etc., Wood Jones gives

an explanation of these malformations which appears to be logical and lucid; but Prof. A. Keith, in an exhaustive examination of all the malformed rectal specimens in the London Museums, and applying comparative embryology to their elucidation, controverts Wood Jones's views in important essentials and adduces strong evidence from comparative embryology to sustain his contentions; in either case, whichever of the two views is ultimately found to be correct, I think it is the imperfect evolution of these cases which is the cause of this peculiar disease, and the imperfection is probably dependent upon pathological processes of an inflammatory or degenerative nature affecting the chorion and embryo.

I will first employ Wood Jones's views in order to make myself clear in the limits of this paper, but feel confident that Keith's method of investigation is the more correct though more difficult of application in a brief paper.

The primitive colon at that level where the peritoneum is reflected forwards (in the adult forming the rectovesical pouch) *ends by opening into the cloaca or urogenital sinus* by an aperture which may be called the cloacal anus, that is, the colon opens into the primitive trigonum of the bladder. *This aperture is guarded by a sphincter.*

From this primitive rectum a finger-like pouch, a *cul-de-sac*, develops backwards towards the tail (the postallantoic gut), represented in the adult by that part of the rectum below the right valve of Houston.

Simultaneously a depression or invagination of the cutaneous structures situated in the perineum takes place, called the proctodeum. This depression forms the anal canal *with the internal and external sphincters of the adult.* Thus,

1. There are two blind *culs-de-sac* approaching one another by their fundi.
2. The primitive colon itself opens by an aperture, the cloacal anus, into the urogenital sinus, represented in the adult by the trigonum of the bladder and the prostatic urethra.

From these data all forms of abnormalities of the rectum and anus can be traced.

Thus the primitive colon may fail to send backwards the *cul-de-sac* which normally forms the adult rectum, and the cloacal anus

may persist, so there is no rectum and the bowel ends by a sphincteric anus opening somewhere into the base of the bladder or the prostatic urethra. If, however, for some cause *the cloacal anus does close* the colon ends at the level of the rectovesical pouch as the blind end; a still further change may take place inasmuch as the blind end of the colon may *atrophy* for some distance upwards, the atrophied portion being represented by a fibrous cord.

Development, however, having successfully passed this stage, the postallantoic gut (*cul-de-sac*) is now formed and projected backwards to meet the proctodeum, while the cloacal anus is obliterated, *but the postallantoic gut fails to meet the proctodeum*. One of two things now follows, either,

1. The postallantoic gut remains as a more or less dilated blind end in the pelvis; or
2. The postallantoic gut *atrophies and the atrophy may extend upwards* and may even involve the primitive colon above the level of Houston's valve (internally) or the rectovesical pouch (externally), and a fibrous cord persists to represent the lower end of the primitive colon and the rectal *cul-de-sac*, a condition differing only from that described in the preceding paragraph in the greater extent of atrophy as represented by the greater length of the fibrous cord.

Thus the colon (sigmoid) under certain of these circumstances *ends in a taper-like extremity* at a somewhat higher level instead of as a blind end somewhere below the level of the rectovesical pouch. It is *this peculiar tapering termination which is copied in the cases of congenital dilatation when it affects the sigmoid*; the taper is situated at, *i.e.*, affects the proper segment of the bowel and is an evidence of the error of development, the various phases and aspect of the degeneration being dependent upon the age of the fœtus and date of onset, possibly, of chorionic inflammation.

I mean by this that the postallantoic *cul-de-sac* may have been successfully projected backwards to meet and fuse with the proctodeum, the cloacal anus may have become obliterated, and *then* the tendency to atrophy may have developed, resulting in this taper-like shape of the junction of sigmoid and rectum.

The dilatation and hypertrophy of the sigmoid is *purely secondary to and consequent on* the malformation, as Keith states that all malformations of the rectum and anus are followed by dilatation and hypertrophy of the bowel above, the intra-uterine youth of the patients enabling the hypertrophy to approximate to a real hypertrophy, *i.e.*, increase of number of elements as well as of size of individual cells and fibres.

Reverting to the cases where the congenital dilatation affects the rectum, that is, the part below Houston's valve or the rectovesical pouch, here one must follow the further development of the postallantoic *cul-de-sac* and its meeting with the proctodeum or perineal depression and fusion of the intervening membranes, resulting in the normal anal canal.

Logically the defect here must be

1. In the postallantoic gut or *cul-de-sac* itself;
2. In the perfection or imperfection of its union with the proctodeum; or
3. In the proctodeum, *i.e.*, the anal canal and its muscles, the internal and external sphincters.

With regard to the postallantoic *cul-de-sac*, which in adults forms the rectum, we know that just above the anal canal there is *normally some dilatation of the rectum called the ampulla*; it requires only an *exaggerated ampulla to produce the picture of dilatation of the rectum*.

When the postallantoic *cul-de-sac* passes backwards it lies dorsal to the situation of the proctodeum, *i.e.*, the anal depression is nearer the pubis while the gut is near the coccyx; and when they meet and the membranes fuse and disappear, the relationship between the anal canal and the rectum is the reverse of what holds in adults, *i.e.*, the rectum passes downwards and backwards, the anal canal upwards and backwards; in other words, the anterior or ventral wall of the *cul-de-sac* near the fundus is fused with the proctodeum, *the actual fundus forming a small pouch posteriorly*—the rudimentary ampulla.

Subsequently the adult normal relationship is assumed. In my opinion the defect resulting in congenital dilatation and hypertrophy of the rectum depends upon the imperfect connection between the postallantoic gut and the proctodeum. I do not mean that a

septum remains, but, for example, possibly the angle of union is abnormal, or the ampulla is too large due to the correct part of the *cul-de-sac* having failed to fuse with the proctodeum: in the former case the *faeces* might not properly engage in the anal orifice and the force of the rectum is uselessly expended in driving the *faeces* against some part of the wall of the ampulla, thus a *functional obstruction exists* and an accumulation occurs; likewise in the case of the exaggerated ampulla, either the *faeces* fail to engage properly in the anal canal, or a portion of the *faeces* remains unexpelled from the ampulla and the collection thus begun is gradually added to.

Further, if the anal sphincters are imperfect the expulsion of the *faeces* from the rectum is not quite complete, a fact which clinical experience teaches to be true, and bit by bit an accumulation occurs, from this cause alone, or associated with the foregoing.

In the two cases here recorded we find in one, on examination of the dissected specimen (see Fig. 11), absence of the external sphincter, or at best a most rudimentary one, and a rudimentary internal sphincter. Clinically both cases possessed sphincters of poor tone even when the rectum had been emptied. Further, in both, on clinical examination one found the accumulation of *faeces* began anteriorly in a part of the ampulla where in a large number of rectums a well-marked recess exists (in the male immediately below the apex of the prostate), so that considerable evidence exists in these cases to support the contentions adduced to explain the disease.

In M. M., who had imperforate anus, one cannot appraise the condition of the rectum previous to perforation of the septum; but Keith indicates that those cases in which the rectum ends blindly near the proctodeum are all dilated, and if this is so that perforation of the septum might have been made at a spot in the rectum not the normal one and this might have led to difficulty in the *faeces* entering the anal canal.

In Keith's view the cloacal anus shifts its position as a result of the development of the sexual organs, as if it slid downwards from the position of the trigonum along the posterior wall of the prostatic urethra, then along the perineum until it meets the proctodeal invagination, with which it fuses and the separating membranes disappear.

In Keith's explanation of the formation of the rectum the malformations of the rectum are easily explained. Assuming the colon opens on to the trigonum, as explained when dealing with Wood Jones's views, the primitive condition may persist or the cloacal anus may close and the gut persist as a blind end at this level, or the anus having closed the colon may atrophy; going a stage further the cloacal opening may have passed downwards to the level of the prostate, or the urethra, or the perineum, or to the neighborhood of the proctodeum and *then closed* and the *colon atrophied*, in any case assuming the conical shape already referred to in dealing with the shape of the sigmoid and rectum when congenitally dilated, and thus bringing Wood Jones's and Keith's explanations into line in endeavoring to explain the origin of the sigmoid variety.

Lastly, when the cloacal anus has reached the neighborhood of the proctodeum it may behave exactly as the *cul-de-sac* in Wood Jones's theory; the intervening membranes may not fuse at the proper time, due to an abnormal or pathological condition of the tissues, and the rectum may remain for a period as a blind dilated end; or they may fuse at an abnormal angle and thus an exaggerated ampulla may form; at least, some interference with the passage of the fæces from the rectum into the anal canal may take place and dilatation and hypertrophy follow, which is the condition of congenital dilatation and hypertrophy.

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SURGICAL PNEUMOTHORAX AS A TREATMENT FOR PHTHISIS

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WHERE pulmonary tubercles that have broken down open into a branch of the air-passages, and are thereby put into communication with the outside, a complication of the greatest importance arises, or rather a new disease; the tubercular process has changed to phthisis; in other words, the patient now carries a wound in the lung, inevitably destined to infection, spontaneous evolution, and automatic extension—an infection much more serious, in the majority of cases, than the original disorder that produced it, and one that it is very difficult to cure.

This distinction is of the first importance, and it is because it has not been clearly and completely made, because a marked division has not been drawn between tuberculosis and phthisis, that the treatment of tuberculosis has been wasting time over such mistakes as attempts to apply specific agents of immunity, tuberculins, and sera, to a quantity of patients who are only accessorially tubercular, but essentially consumptives. Although associated, these two morbid elements differ in nature, evolution, and consequences, and cannot be treated along similar lines. In the strict sense of the term phthisis is an infected external ulcer, that is to say, a surgical disorder.

But it is an ulcer which derives its special and serious characters from its anatomical localization. Although external, it is inaccessible to disinfection by the natural passages; it concerns a tissue that is not dense, is relatively easily attacked, and destroyed, and is, furthermore, very vascular; it is subjected to the constant movements of the organ in which it is seated, whose function is indispensable for life; finally, it is, so to speak, fastened in place through the cohesion of the two pleural folds, which, by preventing the lung from retracting, creates an invincible obstacle to the coming

together of the walls of a cavity as soon as it begins to form, and by means of its force, which is steadily centrifugal, has a tendency, on the contrary, to dilate such a cavity.

In spite of so many unfavorable circumstances, the consumptive, particularly if he is young and placed in surroundings calculated to suppress or reduce infection from the outside, may recover spontaneously; a loss of substance even of some extent may be compensated, and this is of the greatest interest. By observing the method used by nature we are taught in what manner we can help in its purposes and ends.

Now healing of a cavity takes place by the coming together of its walls, which in turn depends on retraction in the corresponding portion of the thoracic framework, on which is seen a depression equal to the internal vacuum that has been done away with. In young patients the chest wall is flexible, and this is why recovery from extensive ulceration is more frequent with them.

The logical inference from this is, that the treatment of ulcerating phthisis should be based on the principle of compression and immobilization of the diseased pulmonary region, and better still of the lung; for it is evident that in view of the physiology of the thorax, partial immobilization is difficult and uncertain. On the contrary, total pulmonary immobilization and even compression may be very easily obtained by the creation of surgical pneumothorax, which respects completely the movements of the other lung, does not require any operation, and may be measured, increased or diminished, at will.

In creating pneumothorax we ought to realize from the start all the conditions necessary for lung cicatrization: juxtaposition of the walls and immobilization of the ulcerocaseous foci; evacuation of the external air and suppression of causes of infection; disinfection even by rapid disappearance of aërobic colonies and of pyogenetic septic resorption; suppression of functional circulation and thereby of the danger of hæmoptysis; suppression of the source of inflammatory complications—in short, transformation of the vast serpiginous ulcer that the lung had become into a dense anaërobic mass similar to a big caseous gland, and not more dangerous to the system than the latter.

These ideas, strengthened by the observation of cases of spon-

taneous pneumothorax with a favorable issue, had already been in my mind for a long time when I ascertained that guided by the same principles an Italian physician, Professor Forlanini, had had the courage to make the practical deduction that they called for, and already for several years had been treating certain classes of phthisis by surgical pneumothorax. I then no longer hesitated to follow his example, and guided by his technic and the results of his experience, which he placed at my disposal at Pavia with the greatest willingness, I began my own attempts. These are at the present time sufficiently advanced to warrant my making the general propositions that are the object of the present paper; I can say from the start that they fully justify the theoretical ideas expressed above.

The researches of Forlanini, although almost unknown in France, have given rise in Italy, America, and Germany to much research, all based on his method. It will not be necessary to give the bibliography on the subject; this can either be found in Forlanini's publications, or in the recent Lyons Thesis of Dessirier. Nor shall I dwell on the apparatus and technic which I adopted bodily from Forlanini without modifications. I shall confine myself to giving my cases and personal conclusions, and in order to do that I shall briefly describe one case in each leading clinical class, accompanying it with the commentary that it seems to require. As the subject is above all a matter of classes of patients, as regards the results as well as the indications, the point of view, number, and statistics present only a very secondary interest.

CASE I.—F. R., a man of 35, was suddenly seized in good health in October, 1907, with very acute symptoms; he reached the Sanatorium, June 4, 1908, with ulcerated, localized, and extensive lesions of the right upper lobe, accompanied by congestion of the base on the same side, subcontinuous fever, and a very precarious general condition. This was no longer a Sanatorium case, and we should have discharged him if after following him for a few weeks we had not thought that this unilateral, rapidly ulcerating form of recent origin and without pleural complications, offered an excellent occasion to use surgical pneumothorax.

On August 2, 1908, a first insufflation of 300 c.c. of nitrogen was made without difficulty in the fifth space on the line of the axilla; this caused neither symptoms nor feverish reaction. Imme-

diately afterwards the screen showed a light, narrow crescent above the diaphragm, somewhat triangular, with an internal base, two centimetres high on expiration; when the patient leaned to the left a light strip appeared along the chest wall, indicating the absence of any adhesive process of the lung.

On August 4 and 7 a litre was injected each time, and we then found that the lung left the wall and the base, and drew near to the stump, although keeping its shape and about a third of its original volume. From this moment the temperature went steadily down; coughing and expectoration, that had been very marked, decreased; and the latter changed its character. The oppression, which was quite severe after each intervention, disappeared in twenty-four hours. On examination the right thorax was dilated and motionless, whereas breathing was increased on the left side. Percussion showed low tympanism at the base, and partial return of sonority at the apex. On auscultation the signs of ulceration were still present, though less extensive and moist; there was obscurity everywhere else. These signs improved progressively. After another insufflation of a litre on August 15, the expectoration decreased to only a little in the morning, the temperature became entirely normal, and the slight gastric disturbance, loss of appetite, and nausea, caused by the pressure on the stomach by the forcing down of the diaphragm, disappeared in its turn.

For nearly a month this improvement continued without further insufflation; but about September 15 the cough, expectoration, and fever began to appear again, and the screen showed that the lung had regained about two-thirds of its size. A series of insufflations of 500 c.c. was then made on September 22, 24, and 30, and October 4 and 8. From that moment all subjective and objective signs disappeared; there was general tympanism, a distant amphoric souffle had replaced all the physiological and abnormal sounds, and the expectoration was mucous in character and contained no more bacilli. The shortness of breath did not increase but, on the contrary, diminished as the patient became accustomed to this new state.

Still, the screen showed the lung hanging like a bag to the spinal column and animated with a few respiratory movements. Since that time it has effaced itself completely, under the influence of new

insufflations; the diaphragm has gone farther and farther down, and a light zone has begun to appear to the left of the spine; we now keep up the pneumothorax by an injection every ten or fifteen days.

At the present time our patient has the appearance of a man in good health; he is gaining in weight, his shortness of breath is decreasing; and save in the case of unforeseen complications there is no reason for thinking that this condition will not continue indefinitely, whatever may be the rapidity of the cicatrizing process during which the pneumothorax will have to be maintained.

This case, to which I could add a similar one, in which there was an enormous cavity, unilateral spreading, with subacute evolution, in a girl, where I also succeeded entirely, quickly and easily, represents the most favorable, not to say imperious indication; for in such instances we can be almost sure to save a patient otherwise condemned to a very early death. The characters of this indication are:

1. A caseous and destructive form of lesion. The degree is of little importance; more advanced and extensive, it gives a more brilliant result, a peremptory demonstration of the fact that the physical condition does not depend on the tubercular infection.

2. Signs of unilateral caseation and cavity formation. It is a matter of indifference that the other side should present signs of closed or torpid tuberculosis, or of diffuse sclerosis.

3. Recent origin of the trouble and exclusive localization to the lung tissue; in particular, absence of pleural complications and adhesions, revealed at stethoscopic examination by the mobility of the marginal portion of the lung, and on the screen by transparency of the non-infiltrated zones.

In a case of this sort, application of the method is extremely simple; but the first insufflation must, as Forlanini had advised, be prudently made, on account of possible accidents, to be referred to later, although they are unusual in this form. The needle, mounted on Forlanini's syringe, must therefore be carefully inserted to a depth of 2 or 3 centimetres according to the fleshiness of the patient on the line of the axilla; it should then be pushed very slowly, with an eye on the manometer, whose sudden fall indicates that the point has entered the pleural vacuum. If this fall does

not occur suddenly, it is necessary to feel around a little, although moving the needle as little as possible, especially in a lateral direction, in order not to start any pleural reflex. After first making sure, by means of the syringe, that the point is not in a vessel, the insufflation can be begun by opening the communication with the reservoir of nitrogen. When the pleural cavity is healthy, insufflation is easy, and the aspiration that takes place makes the blowing apparatus superfluous.

When 150 to 200 c.c. have passed into the pleural cavity, it is prudent to stop; the patient should then be examined with a screen, to observe the particularities of the operation and the lack of adhesions. There is then no reason why total pneumothorax should not be accomplished more rapidly than in the foregoing case, for instance in two or three sittings, four or five days apart; the cavity is made, and the insufflations can be performed with simple needles without drawbacks.

Each operation, however, should be followed by screen examination, whose help is indispensable, and which alone supplies exact information as to the completeness of the pneumothorax, lung mobility, disappearance of the cavities, and descent of the diaphragm, and indicates the exact point at which to stop in increasing the pneumothorax and at which to content ourselves with maintaining the ground gained. For it may happen that physiological and morbid sounds may be replaced at auscultation by those of pneumothorax, and yet the screen may show a lung reduced to a slight size, but still moving to breathing; now it is necessary for success that during the time required to transform the pathological tissue into a cicatricial mass, the lung should be motionless and even somewhat compressed. This state has been acquired when the organ can be no longer distinguished, and when the light of the pneumothorax appears on the other side of the spine.

The presence of this gas occupying the half of the thorax at a pressure somewhat greater than that of the atmosphere, naturally has a certain effect on the neighboring organs. When the pneumothorax is on the left side, displacement of the heart and aorta is very marked and may reach complete dextrocardia; for this reason insufflation must in these instances be more carefully performed and the pneumothorax must be increased less rapidly.

The lowering of the diaphragm, which becomes very marked when the retractile power of the lung has ceased and we endeavor to compress it, gives rise by pressure on the stomach to temporary gastric disorder, of which it is well to know the cause—disorder that is slight, and without importance. It consists in a slight intolerance to any quantity of food, manifesting itself by loss of appetite, rapid satiety, fulness after meals, and even vomiting. This distress may be very marked the first few days after air insufflation; if it becomes really troublesome, nothing is easier than to put an end to it by extracting a certain quantity of gas.

I will merely mention among the ordinary incidents of this treatment, subcutaneous emphysema, that may occur either during actual insufflation or later on, by the nitrogen compressed in the thorax seeking issue through the orifice made by the needle. This little complication is of no importance; it is sufficient, to avoid it, to use fine needles, except for the first treatment, which is greatly facilitated by the use of a larger one offering little resistance to the passage of the gas, enabling us to estimate more easily any variation in intrathoracic pressure, and facilitating in this way access to the pleural vacuum.

The case related above is not only the type indicating operative procedure, but it also serves as a model to illustrate easy technic and rapid success. Still, the method is applicable to other patients besides these, although we shall now have to deal with a new factor, pleural adhesions, of which it is easy to understand the great importance. When the adhesive pleurisy is complete, as happens in certain cases, it manifestly creates an insurmountable obstacle to pneumothorax; but it can also exist partially in all degrees, and according to the age and degree of organization of the adhesions, may show itself more or less surmountable. This gives rise, then, to a whole category of cases in which although pneumothorax is indicated by the form and nature of the lesions, its realization is more or less easy and possible. Clinical examination and the screen lead us to suspect the difficulty, but except in the cases where parietal retraction reveals total obliteration of the pleural cavity the difficulty may not be insoluble. Nothing but actual trial will settle the question; as this trial, however, is not free from risks, it demands patience and a prudent technic. Of this I will give two examples in increasing order of technical difficulty.

CASE II.—Miss B. M. had extensive, localized, ulcerated lesions that began insidiously early in 1907 with attacks of pleurisy that did not require puncture, and progressed regularly until her arrival at Hauteville in April, 1908. Her general condition had remained good, but she had slight fever, frequent cough, and abundant expectoration with bacilli. The left lung appeared healthy, with the exception of intermittent pleural rubbing at the top; at the right apex there were metallic râles, souffles, bronchophony, etc., coming down below the spine of the shoulder blade behind. Hygienic treatment reduced the fever a little, but had no effect on the objective symptoms, and surgical treatment was decided on.

On July 30, at the first attempt to perform insufflation, the needle penetrated 5 centimetres in the right axillary region, fifth space; the puncture was a little painful, the gas did not seem to enter freely, only 200 c.c. were injected; slight febrile reaction followed. On August 1, at the second attempt, the gas entered much more readily, but had to be stopped at 100 c.c. on account of partial syncope; very slight febrile reaction followed. On August 3, after some difficulty, a third injection of 500 c.c. was followed by some pain in the side.

The same day, after the third injection, the patient showed on the screen a light triangular zone above the diaphragm extending from the spine to the side and about 2.5 centimetres high. The lower edge of the lung could be readily seen, and the diaphragm appeared higher on the right side than on the left.

On August 6 and 11, injections of 1,000 and 500 c.c. were made. Auscultation sounds began to disappear, and obscurity increased in the region of the base where sonority made its appearance; but the screen showed that nothing but the space above the diaphragm was perceptible, the lung remaining adherent to the lateral wall, and the expectoration continuing as abundantly as ever. The treatment was then suspended for a month, after which it was resumed with a series of insufflations, September 23, 500 c.c.; 26, 500 c.c.; 30, 500 c.c.; and October 5, 1,000 c.c. were injected. Shortness of breath then became very marked, the right chest was dilated, 44 cm. as against 40.5 on the left; the cavity-suffle disappeared at the apex; and the lower zones presented tympanism. The screen then showed

two big adhesions with large pedicles; the one uniting the external third of the diaphragm to the chest wall; and the other this wall to the external wall of the lung, whose retraction it impeded. The lung was nevertheless forced over against the spine and completely effaced in its upper portion.

From that time on an injection was made every week in gradually decreasing quantities. At the end of November the adhesions became more and more restricted, the lung disappeared, and the characteristic luminous zone could be seen to the left of the spine. At the same time the subjective signs diminished, the oppression was more marked, the appetite slight, and the sputa, which were fluid, no longer contained bacilli. At auscultation, complete pulmonary silence, tympanism, and amphoric sounds were heard; while to the left, there was very noisy breathing.

At the present time the temperature is perfectly normal, and the weight is increasing; an insufflation, from 300 to 500 c.c., is made every twenty days to maintain the pneumothorax.

If we estimate the amount of nitrogen used with this patient to obtain total pneumothorax, we see that after deducting the quantity probably absorbed, which experience has shown to be about a litre per month at the beginning of the treatment, though this diminishes later on, we find that it is considerably more than would be accommodated by the normal pleural cavity; hence we conclude that some of the insufflations made at the zone of adhesions must in reality have passed into the lung. This is an incident difficult to avoid, in cases of extensive parietal adhesions; it is also difficult to diagnose, as the flow of gas takes place quite as easily into the lung as it does into a pathological pleural cavity shut in by adhesions that are not easily stretched. Again, the water manometer, whose initial fall and subsequent variations, corresponding to the respiratory movements, are so characteristic during operations when the pleural membrane is normal, remains, on the contrary, motionless when the insufflation passes into a pathological pleural membrane or into the lung; it is even frequently the case that pressure is lower and respiratory variation more marked in the lung than in the pleural cavity. It is therefore quite difficult to be sure in doubtful cases just what region has been reached by the needle; nothing but an examination with the screen enables us to form an opinion. But in-

trapulmonary insufflation does no harm, provided that the precaution has been taken to make sure, by means of Forlanini's safety exploring syringe, that the point of the needle is not in a vessel. It is scarcely necessary to add that it is desirable to puncture in regions which previous experience, combined with the screen examination, has shown to be safest, though even in this rule there is nothing absolute, since the change of place produced by gas pressure constantly alters the pleuropulmonary outline.

The technical difficulties encountered in the preceding case were even more pronounced in the following one.

CASE III.—Miss M. B. had an extensive, localized, ulcerative process of the left apex that began two years ago; there was no lesion on the right, but the base was infiltrated, and there was marked thoracic retraction over the whole lung, and particularly at the base. The indication was therefore evident, but the operative prognosis very uncertain.

Between Oct. 24 and Nov. 26, we made in this case twelve insufflations, representing a total amount of 9800 c.c., and it was only at the end of this time that we were able to produce the luminous crescent with concavity formed by the pericardium. The lung was adherent from top to bottom; and adhered in addition to the median portion of the pericardium over an extensive, very dark surface, the pedicle on the pericardium, whereas the base of the pericardium spread like a fan over the inner surface of the lung. It was evident here that the majority of our insufflations had gone into the lung, and pneumothorax had only been produced by traversing the outer cortical zone and reaching some deep free space, probably in the interlobular pleura. Success, therefore, which was here a mere matter of chance, was due entirely to our perseverance and varied attempts; but once the pleural cavity was opened at one point, the volume of the lung decreased, and it was then easy by means of a series of small injections made at intervals of two or three days only, to produce pneumothorax; we then saw the adhesions stretch and grow thin and transparent, traversing with their ramifications the vacuum created by the operation, while at the same time the heart, aorta, and mediastinal organs gradually went over almost entirely to the right side. All of this work was accomplished without other subjective phenomena than a little tinged sputum due no doubt to lung

punctures, and, after each successful injection, shortness of breath and pain in the side caused by the stretching of the adhesions. The diaphragm, fastened up by strong bands, showed no tendency to descend, and no digestive trouble occurred with this patient, nor were there any cardiac or circulatory modifications.

During this treatment, and on account of the lung tissue adhering to the wall and of the central position of the artificial cavity, the ordinary stethoscopic modifications did not take place; nothing was of assistance at first but the screen examination, and the increase in chest-perimeter subsequently enabled us to estimate the advance in the artificial pneumothorax.

At the present time the technical result has been accomplished, and the open cavities with which the lung was honeycombed are replaced by extrapulmonary cavities that are closed and filled with a sterile gas.

This case seems to represent the utmost limit of the pneumothorax treatment; it shows that the method can be employed in spite of vast adhesions, provided these are not too old and can be made to give way. Nothing but trial enables us to decide in such a question, and if the attempt is well tolerated it must be repeated without hesitation before deciding against it. When a first partial result has been obtained it is necessary to proceed by means of small but frequently repeated injections, so as to stretch the adhesions patiently and continuously.

But it may happen that the adhesions are of long standing, resistant, and cannot be broken down. We must then know when to abandon attempts that are not without danger; this leads us to say a few words concerning the serious accidents connected with the method, but which I shall only mention, as they have been recently completely studied in one of Forlanini's publications.

In the first rank comes intravenous injection of nitrogen, with consequent cerebral gaseous embolus. This accident, which is very serious and has proved fatal, is very much to be apprehended when we remember that the connective tissue of old adhesions is very vascular. But we can guard ourselves against it almost with certainty by the use of Forlanini's syringe mentioned above, which enables us to explore the region that the point of the needle has reached before insufflation: if blood is aspirated its position must be changed.

It sometimes happens, as in our third case just mentioned, that aspiration brings back a little serum from a pleural pocket; this is evidently of no consequence, but shows that the needle is in the right place.

A second class of accidents, more difficult to avoid, consists in the reflex, nervous disorders due to operating on the pleura and designated by the term pleural eclampsia. I witnessed an accident of this sort, quite serious, under the following circumstances. I wished to create artificial pneumothorax in a patient of 50 in a very weak condition, with subacute tuberculosis of the whole left lung and intense congestion of the base. I made three attempts at different times, but failed in each one of them. At the first two attempts the operation tried the patient manifestly; he seemed on the point of fainting, was short of breath, but still there was nothing very characteristic. On the third, after three unsuccessful punctures I was preparing for a fourth when suddenly the patient fell back with congested face, eyes fixed and glassy, pulse weak and rapid, and breathing labored, but completely conscious and complaining of paralysis of the lower limbs, thoracic tightness, and uncertain sight. This very alarming condition lasted nearly an hour; during the three following hours the signs disappeared gradually, though the temperature rose to 40° C. The following day all trace of the event had disappeared. I cannot refrain from mentioning, though without drawing conclusions, that I was struck by the analogy of this incident with certain serum accidents observed during attempts at antitubercular serotherapy.

I have only met with complications of this sort on this occasion; but I have been forced, on the other hand, to interrupt an insufflation a number of times on account of more or less menacing signs, a species of aura difficult to describe, as it consists entirely in subjective distress that the patients are quite unable to render an account of.

Occurrences of this sort are impossible to foresee; they have, though, certain predisposing causes: in the patient, a weakened condition, apprehension, and previous mishaps of this kind; in the operator, it has seemed to me manifest that repetition of the puncture at one *séance*, movements of the needle during puncture liable to damage the pleura, the use of large or badly-polished needles,

finally, and specially, the pressure of numerous adhesions and of inflammatory processes increasing the local irritability of the pleura, are likely to predispose to mishaps or to increase their importance. But in all events the injection of gas is not to blame; it is manifestly the operation on the pleura that gives rise to these reflex symptoms, which may, in certain cases, cause cardiac and respiratory paralysis, followed by death. We cannot therefore be too much on our guard against them. Punctures should be interrupted at the slightest distress, and the greatest prudence should be observed in using the method in unfavorable cases, in weakened patients, and particularly with those who have manifest and active inflammatory signs in the pleura, such as febrile congestion of the base, for instance.

It is with intention that I have given a somewhat schematic character to the description of this method. It appeared to me that the most important point was to bring into relief the essential elements of the question, and above all to lay stress on the indications for the method, in the treatment of serious advanced cases of phthisis that are not amenable to any other treatment, since it is in such cases that Forlanini's method is chiefly indicated, and since it is of the greatest importance that we should no longer deprive ourselves of so rational and so powerful a help.

This, however, does not mean that the use and efficacy of the method end there. I have, no doubt, appeared to consider it as the best treatment for phthisis, as opposed to closed fibrous pulmonary tuberculosis that is amenable to specific treatment, and such is in fact my belief; but it would be certainly not illogical, and Forlanini is now working at this side of the question, to apply pulmonary immobilization to unilateral tuberculosis even in forms that are fibrous or have a fibrous tendency, provided they be progressive, besides applying it regularly to the other localizations of the same infection.

Serious and repeated hæmoptysis is also a formal indication for pneumothorax, which by suddenly suppressing the functional circulation of the lung cannot fail to have on the hæmorrhage the radical action of a ligature; when in such cases there is urgency, total pneumothorax must be induced from the start. Through an involuntary and enforced delay of a few days I lost a patient

from fulminant hæmoptysis just as I was preparing to carry out the operation.

Finally, the motives which justify and indicate the use of surgical pneumothorax in phthisis are equally applicable to all cases of suppurating pulmonary cavities, and particularly to unilateral bronchial dilatation of the base, whose gravity depends on the same causes as those of phthisis. Unfortunately it is rare that such lesions, when they are a little ancient, have not given rise to an inflammatory process in the neighborhood, and are not accompanied by pleural symphysis. An attempt that I made in a case of this kind failed on this account, and since then I have not had an opportunity to try again.

The results of the method as they now stand are highly satisfactory, and we can say without further delay that confined even to its most evident and formal indications, and only to suitable cases, it places in our hands a means of curing, at least of the lesion proximately fatal, patients otherwise condemned to a rapid and certain death.

I have passed over in silence, not having yet sufficient personal experience, the question of the duration to be given to the artificial pneumothorax, and of the line of conduct to be followed after the check and healing of the lesions, relative to the possible re-expansion of the lung. These points have been treated by Forlanini, who in spite of favorable secondary evolutions and final recoveries, concludes, for reasons of security and æsthetics, in favor of prolonging the pneumothorax for a very long while.

THE PRESENT STATUS OF THE CAMMIDGE REACTION

BY EDWARD H. GOODMAN, M.D.

(From the private laboratory of Dr. John H. Musser)

AFTER having been practically ignored for several years, the pancreatic reaction, first described by Cammidge and now generally called the Cammidge reaction, seems at present to be attracting attention throughout the medical world. The attitude of the writers toward the test has apparently changed, and recent papers show the total absence of that hostility which was so characteristic of the earlier communications. Instead there has come with time a more scientifically critical approach of the subject, and work is now being done on the fundamental principles so far neglected by Cammidge, namely, the chemistry of the reaction and its production experimentally. It is to present a compilation of recent work along clinical, chemical, and experimental lines that is the object of this paper.

Historical.—Cammidge¹ in 1904 reported before the Royal College of Surgeons the result of work which he thought would prove of value in the diagnosis of pancreatic disease. The theory on which he based his investigations was grounded on the pathological condition known as fat necrosis, generally seen in acute but not uncommonly in chronic inflammations of the pancreas. He believed that even when no visible evidence of fat necrosis presented itself, there were some "molecular changes" in the blood which might be demonstrated by chemical means. It is generally held that the masses of fatty acids, or the calcium salts of the same, make up the lesion known as fat necrosis, the other constituent of the fat, that is, the glycerin, being absorbed into the circulation. As the changes seen in the blood of patients suffering with pancreatitis resembled in certain respects the alterations observed in animals after the subcutaneous injection of glycerin, Cammidge believed the demonstration of glycerin in the blood would be of assistance in diagnosing pancreatic lesions. Owing to the many objections in-

herent in any chemical examination of that fluid, and recognizing the selective action of the kidneys for abnormal ingredients of the blood, the examination of the blood was abandoned and the urine was tested for glycerin or its derivatives.

The method first employed has been named the "A reaction," and was conducted as follows: 10 c.c. of clear filtered urine are boiled on a sand-bath for ten minutes with 1 c.c. of concentrated hydrochloric acid (sp. gr. 1.16), a small funnel being placed in the neck of the flask for condensing purposes. Five c.c. of the original filtered urine and 5 c.c. of distilled water are then added to the contents of the flask and the latter cooled in running water. Four grammes of lead carbonate are slowly added to neutralize the excess of acid, and the flask allowed to stand for a few minutes to complete the reaction; the flask is again cooled in running water and the contents filtered through a well-moistened, close-grained filter paper. The filtrate, which must be perfectly clear, is made up to 15 c.c. with distilled water and to this are added 2 Gm. of powdered sodium acetate, 0.75 Gm. of phenylhydrazine hydrochloride, and 1 c.c. of 50 per cent. acetic acid. After gently boiling on the sand-bath for five minutes, the mixture is poured hot into a test tube, made up to 15 c.c., and allowed to cool spontaneously. At the end of twenty-four hours, or earlier if the case is a severe one, a more or less abundant flocculent yellow precipitate is seen, which when examined microscopically with a 1/6 inch objective is found to consist of sheaves and rosettes of golden-yellow crystals.

After using the test in a number of instances, Cammidge observed that the crystals varied in type in various lesions of the pancreas, and positive reactions were also obtained in other diseases, such as cancer, adenitis, and pneumonia. To remedy this apparent invalidation of the usefulness of the method, a second reaction was devised and called the "B reaction." "This differentiating test depends upon the fact that the formation of crystals described in reaction 'A' is interfered with, in inflammation of the pancreas, by a preliminary treatment of the urine with perchloride of mercury, while such treatment does not affect the appearance of the crystals in cases of cancer of the pancreas and other conditions which give rise to a positive reaction." The method of performing the "B" reaction is as follows: 10 c.c. of filtered urine are mixed with

10 c.c. of a saturated solution of perchloride of mercury, and after standing for a few minutes the mixture is filtered through well-moistened filter paper, and to 10 c.c. of the filtrate, 1 c.c. of concentrated hydrochloric acid is added. This is boiled on a sand-bath for ten minutes, and diluted with 5 c.c. of the mixed urine and mercuric chloride plus 10 c.c. of distilled water. After cooling in running water the excess of acid is neutralized with lead carbonate and the rest of the procedure carried out as in reaction "A."

Certain objections from the side of chemical technic will be discussed later; but as a result of these Cammidge abandoned his "A" and "B" reactions, and published work on a new reaction, or "reaction C," which he claims gives accurate results in competent hands.²

A portion of the twenty-four hours' urine or a portion of the mixed night and morning specimens is examined for albumin and sugar. If albumin is present, it is removed by boiling with the addition of a few drops of acetic acid, and filtered. The removal of the sugar will be spoken of later. To 40 c.c. of the filtered, albumin-free, acid urine are added 2 c.c. of concentrated hydrochloric acid, and the mixture gently boiled on the sand-bath for ten minutes following the first evidence of ebullition. A small flask with a funnel as condenser is used for the purpose. After ten minutes' boiling the flask is removed from the sand-bath, cooled in a stream of running water, and the contents made up to 40 c.c. with distilled water. Eight grammes of lead carbonate are then added to neutralize the excess of acid, and after standing a few minutes the flask is again cooled in running water and the contents filtered through a moistened, close-grained filter paper.*

At this stage of the procedure, if sugar has been found on qualitative analysis, a portion of yeast is added to the clear filtrate, and the flask placed in the incubator over night. The next morning the solution is filtered and the test is continued.

The acid filtrate is thoroughly shaken with 8 Gm. of tribasic lead acetate and the precipitate removed by repeated filtration through a well-moistened, close-grained filter paper. To get rid of the excess of lead, 4 Gm. of powdered sodium sulphate are added,

* I have found the most satisfactory paper to be Schleicher & Schull No. 589, Blue Ribbon.

the mixture heated on a wire gauze to the boiling point, cooled in running water to as low a temperature as possible, and the precipitate removed by careful filtration. Ten c.c. of the filtrate are put in a small flask, made up to 17 c.c. with distilled water, and to this are added 0.8 Gm. of phenylhydrazine hydrochloride, 2 Gm. of sodium acetate, and 1 c.c. of 50 per cent. acetic acid. The flask is then fitted with a funnel condenser and gently boiled on the sand-bath for ten minutes, at the expiration of which time it is filtered hot through a filter paper moistened with hot water. The filtrate, if necessary, is made up to 15 c.c. with hot distilled water, and the whole well stirred with a glass rod.

"In well marked cases of pancreatic inflammation, a light yellow, flocculent precipitate should appear in a few hours, but in less characteristic cases it may be necessary to leave the preparation over night before a deposit occurs. Under the microscope the precipitate is seen to consist of long, light yellow, flexible, hair-like crystals arranged in delicate sheaves, which when irrigated with 33 per cent. sulphuric acid melt away and disappear in ten to fifteen seconds after the acid first touches them. The preparation must always be examined microscopically, as a small deposit may be easily overlooked with the naked eye, and it is also difficult to determine the exact nature of a slight precipitate by macroscopic investigation alone" (Cambridge, *loc. cit.*, p. 253).

Chemical.—Ham and Cleland³ criticize Cambridge's work very severely, and claim to have found positive crystals in all urines, depending on the concentration, this in turn being determined by the degree of ebullition. A second contention was that the pancreatic crystals are nothing more or less than a compound of lead with phenylhydrazine. A third and a very just criticism was occasioned by the statement by Cambridge that crystals of acute pancreatitis are soluble in strong sulphuric acid in $\frac{1}{2}$ –1 minute, whereas in chronic pancreatitis the time will be longer, and in malignancy the process will take three to five minutes. As the crystals in each case are supposed to be derived from the same mother substance, Cambridge's claim seems hardly tenable, nor does Cambridge defend his position any too well (*Lancet*, 1904, i, p. 1459).

Willcox⁴ asserted that normal urines after hydrolysis with

hydrochloric acid give a positive reaction, and concludes that "normal urine invariably contains some substance, a polysaccharose or glycoprotein perhaps, which itself gives no characteristic crystals with phenylhydrazine, but which after hydrolysis always yields a substance (probably a sugar), which latter substance gives very characteristic crystals with phenylhydrazine."

In reply to this Cammidge points out that the method used by Willcox is not the one advocated by Cammidge, and that Willcox's conclusions are to be judged accordingly.

Schroeder ⁵ and Haldane ⁶ have criticized Cammidge in as much as they were not able to prove the existence of glycerin in the urine. The theory of glycerin, Cammidge points out in reply, was only held as a working hypothesis, and has been given up by him.

The view now held by Cammidge is that the substance forming a precipitate with the phenylhydrazine is a pentose, not present in the urine as such, but formed from the mother substance, whatever that may be, by hydrolysis. As the pancreas contains 2.48 per cent. pentose, about four and a half times as much as is found in the other organs, this would point to the pancreas as being the most likely source of the mother substance. Cammidge does not think that glycuronic acid can be the cause of the reaction, for he believes he removes it entirely by means of tribasic lead acetate.

Eichler ⁷ seems to have been the first to report any work along strictly chemical lines. He determined the melting point of the crystals obtained after experimentally induced pancreatitis, and found it to be 182° C. He did not make any further researches with the body, only stating that 182° C. is not the melting point of the osazone of either glucose or glycuronic acid.

The most important work in this direction has been recently reported by Caro and Wörner.⁸ They examined the crystals from the urine of a case of pancreatitis and found the melting point to be between 150° and 160° C. As the phenylhydrazine compound of glycuronic acid has a very similar melting point, they tried to obtain the parabromphenylhydrazine compound of glycuronic acid from the urine. Their product was a body with a melting point of 226° C., whereas Neuberg's body melts at 236° C. The determination of the specific rotation as advocated by Neuberg could not be made owing to the small quantity of crystals obtained, but the

authors believe the substance is glycuronic acid. They do not, therefore, agree with Cammidge that the acid is thrown out in the "C" reaction, and advise in all instances the determination of the melting point together with isolation of the crystals by means of parabromophenylhydrazine.

In the course of my clinical and experimental studies, I have not gone into the chemistry of the reaction. In only one case of experimental pancreatitis did I determine the melting point. This was not sharp, but appeared to be about 155°C .

The question of the chemical nature of the reaction must be regarded as undecided, although recent work points to glycuronic acid as being the cause. It is to be hoped that Cammidge's future work will shed some light on this very important feature of his test.

Experimental.—Strangely enough, Cammidge has so far reported no work with his method based on animal experimentation. Eichler⁷ made three experiments on dogs and was convinced of the usefulness of the test; but as he used the "A" and "B" reactions, and as these reactions have been unfavorably criticised, his work may be questioned to a certain extent. The first work done on the Cammidge reaction in experimental pancreatitis, using the "C" reaction, has recently been published in a preliminary report by Speese and Goodman.⁹ Two types of pancreatitis were induced, a hemorrhagic pancreatitis by injection of cotton-seed oil in the pancreatic duct, and a pancreatitis of the chronic type by ligation of the duct of Wirsung. Studies were made of the urine before operation and at various times following the operation, and in each case post-mortem studies were made of the macroscopic and microscopic appearance of the gland. Eight animals (dogs) were studied, five for acute hemorrhagic pancreatitis, three for lesions of a more chronic type. In four of the first series of dogs, positive crystals were found after operation, while in one they were missed. In this last instance, however, a post-mortem examination revealed a normal pancreas (macroscopic and microscopic examinations), the attempt to inject oil into the duct having been unsuccessful.

All of the three dogs constituting the second series exhibited positive crystals, which in one case disappeared for a few days and then reappeared. An explanation of this phenomenon is not given by the authors.

Quite recently Eichler and Schirokauer¹⁰ reported some experimental work which led them to an indefinite opinion regarding the value of the test. In five dogs there were no typical crystals observed, and in five other dogs the appearance was irregular and sporadic. Their work seems to the writer to have been conducted along no definite line and the nature of the lesion they produced was obscured by one or more varieties of insults to the pancreas.

In a personal communication Cammidge has informed the writer that he has been studying the reaction from the chemical and experimental sides and his publication will be awaited with much eagerness.

Clinical.—After the criticisms raised by Ham and Cleland,⁸ Schroeder,⁵ Gruner,¹¹ Willcox,⁴ and Haldane⁶ against the "A" and "B" reactions, it was hardly to be expected that the "C" reaction would attract much attention. Cammidge himself has published his results in 250 cases, of which 175 were negative. Fifty of these were normal urines; 92 miscellaneous with no data; 11 cases of gall-stones in the gall-bladder, 10 of gall-stones in the common duct, both conditions accompanied by pancreatitis; and 12 out of 16 cases of cancer of the pancreas. Only 2 cases of acute pancreatitis were studied, both of which gave positive reactions; and in no case of chronic pancreatitis *per se* or accompanied by gall-stones was a negative reaction observed.

During the past year there have been several papers published on results with the improved, or "C" pancreatic reaction.

Watson,¹² after a study of 120 consecutive cases, believes the test will prove of value to physicians in the diagnosis and treatment of pancreatitis, although he has found positive reactions in a large variety of dissimilar conditions.

Schroeder¹³ concludes from his studies that inflammatory and destructive diseases of the pancreas may give rise to certain bodies belonging possibly to the sugars or related compounds, although the reaction is not to be considered as pathognomonic for diseases of the pancreas.

After a study of 32 cases, Röth¹⁴ believes the reaction possesses no real diagnostic value, as he found typical crystals in many varieties of diseases.

WRITER'S CASES

	Number	Positive	Negative
Acute pancreatitis	1	1	0
Chronic pancreatitis	9	7	2
Carcinoma of pancreas	5	1	4
Carcinoma of pancreas secondary to carcinoma of stomach	2	1	1
Carcinoma of stomach	6	0	6
Sarcoma of stomach	1	0	1
Gastric ulcer	5	0	5
Hyperchlorhydria	6	0	6
Gastroptosis	1	1	0
Gastritis	3	0	3
Cirrhosis of liver	13	0	13
Cholangitis	1	0	1
Abscess of liver	1	0	1
Cholecystitis	5	0	5
Jaundice, obscure origin	1	0	1
Gall-stones with arteriosclerosis of pancreas	1	1	0
Gall-stones with pancreatitis	3	2	1
Gall-stones without pancreatitis	7	0	7
Carcinoma of gall-bladder	3	0	3
Enteritis	1	0	1
Obscure abdominal tumor	2	0	2
Fibroid of uterus	1	0	1
Autointoxication	2	0	2
Intestinal obstruction with glycosuria (no operation)	1	1	0
Diabetes mellitus	16	3	13
Nephritis	1	0	1
Eclampsia	1	0	1
Tuberculous peritonitis	1	0	1
Appendicitis	1	0	1
Cancer of rectum with metastases to liver	1	0	1
Pernicious anemia	1	0	1
Arthritis deformans	1	0	1
Myocarditis	1	0	1
Suspected pancreatitis (no operation)	3	0	3
Total	108	18	90

I have made between 150 and 200 examinations, including the purely clinical cases and the cases of experimental pancreatitis. One hundred and eight separate cases have been examined, and for the most part these have been cases where the differential diagnosis of pancreatitis had to be considered. The diagnosis in all the cases of chronic pancreatitis, carcinoma of the pancreas, and gall-stones

was confirmed by operation or autopsy, while the case of acute pancreatitis died with all the classical symptoms of the disease, so here one may be reasonably sure of the correct diagnosis, even with no post-mortem control. It will be seen that of the 108 cases, 18 gave a positive reaction, and of these 18, the diagnosis of 12 was made or confirmed at operation.

Nine cases of chronic pancreatitis were studied, 7 being positive and 2 negative, a slightly different result from that obtained by Cammidge, but still very convincing.

Of 7 cases of carcinoma of the pancreas, primary or secondary, 2 gave positive reactions, or about 29 per cent., agreeing with Cammidge.

One case of gall-stones with pancreatitis gave a negative test.

All of the 12 positive cases confirmed by operation were seen in some lesion of the pancreas. On the other hand, excluding carcinoma, 3 cases in which the pancreas was diseased gave negative reactions.

Positive crystals were found in one case of gastropexia with clinical symptoms of pancreatitis.

The patient in whom the diagnosis of intestinal obstruction was made had glycosuria and a positive reaction. The nature of the obstruction could not be determined, although the surgeon in charge suspected a malignant growth of the intestines with secondary invasion of the pancreas.

Of 16 cases of diabetes studied, 3 gave typical crystals; in 2 of these the diagnosis of pancreatitis could not be excluded, while the third seemed to be a pure case of diabetes mellitus.

Being interested in the question of alimentary levulosuria in cirrhosis of the liver, 13 cases were studied for the Cammidge reaction. Steinhaus¹⁵ has objected to the use of levulose as a test of hepatic insufficiency, on the grounds that chronic pancreatitis is usually associated with the cirrhosis, and he believes the poor utilization of the sugar is due to this rather than to the hepatic lesion. It will be seen that none of my cases was positive with Cammidge's test, and owing to the almost constant occurrence of positive crystals in pancreatitis, I prefer to regard the levulosuria as due to the impaired glycogenic function of the liver rather than due to any other cause.

CONCLUSIONS

1. The chemical nature of the crystals is not known, but recent investigations would seem to indicate that they are the osazone of glycuronic acid (Caro and Wörner, *l. c.*).

2. Experimentally it has been shown that the reaction is almost constantly associated with lesions of the pancreas (Speese and Goodman, *l. c.*).

3. The clinical value of the reaction seems assured.

4. The test is not pathognomonic, but taken in connection with the clinical history and other laboratory findings, it is strongly suggestive of pancreatic disease.

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THE TREATMENT OF ABSCESS IN HIP DISEASE WITH A REPORT OF CASES

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MUCH has been said and written on the treatment of abscess occurring in the course of hip disease, yet the propriety of surgical interference, the indications for it and the methods to be employed are still mooted questions.

In a critical study of the papers upon the operative treatment of the symptomatic abscess in hip disease, presented during the past twenty years before the American Orthopædic Association, which may be conceded to embody the experience of the most eminent Orthopædic Surgeons of this country, we find the most diverse opinions, fortified by statistics, which might well confuse the seeker after truth in this field of Orthopædic Surgery.

Statistical studies upon this subject are up to the present not exhaustive enough and probably not sufficiently numerous to permit of definite conclusions. The general condition of the patient, the virulence of the disease, details of technic and subsequent treatment, whether the patient be a hospital case and therefore in an unfavorable environment as compared with well managed private treatment, all these and many more details must enter into statistical studies bearing upon the operative treatment of abscesses, but as yet these data are either entirely wanting or incomplete and therefore a detailed review of the literature would be a confusing task and productive of but few well established facts. Suffice it to say that we have three courses to choose between, namely, prompt evacuation as soon as a collection of tuberculous fluid becomes palpable, absolute non-interference, and finally, incision and evacuation upon certain definite indications.

The causes of this diversity of opinion are many, but we find that the crucial point upon which the question of non-interference or of prompt surgical intervention revolves is primarily the danger and frequency of causing a mixed infection of a cold abscess as a result of operative measures and the prognosis of a case when such a complication has set in.

In this paper I propose to consider some phases of this disputed question, devoting my attention mainly to the dangers involved in indiscriminate operative interference with the so-called "sterile abscess" in hip disease.

General Considerations.—Surgical measures in the treatment of abscess in hip disease must be based upon a clear understanding of the pathology of abscess formation and of its course, of its effect upon the underlying bone disease, the frequency of and dangers involved in engrafting a mixed infection upon an already existing tuberculous lesion and the dangers arising from it when not interfered with.

Of the pathology of abscess in hip disease only a few general remarks are here necessary. The tuberculous process after being established in the epiphysis successively invades the articular cartilage, the membranes of the joint and the joint capsule. Ultimately the capsule ruptures and the disease extends into the peri-articular structures. In this process the tissues invaded undergo caseation and liquefaction necrosis and thus a cavity is formed, various in extent and shape and containing semifluid cheesy material, the so-called tuberculous pus. This constitutes the sterile abscess which enlarges in the line of least resistance and which unless controlled by treatment or if the disease be of a destructive nature, soon reaches the surface, breaks through the overlying skin and results in spontaneous evacuation by the formation of a sinus. In some few cases an abscess may make its appearance in the peri-articular structures before the disease has involved the joint cavity.

The wall of this cavity is made up of tuberculous granulation tissue, and it is within this wall that the tubercle bacilli are found, and for this reason examination of the contents of such an abscess shows in the majority of cases the absence of bacteria, unless mixed infection has occurred, and in only a few cases can the presence of tubercle bacilli be demonstrated microscopically. Centrifuging

of the pus and inoculation experiments into animals will disclose the presence of active tubercle bacilli in a larger proportion of cases than will be revealed by microscopic examination. In some cases the contents and even scrapings from the wall of a tuberculous abscess may be entirely negative to both microscopic and bacteriologic examination, in which case it is probable that the abscess in the periarticular structures has become entirely occluded from the focus of disease and that the tuberculous process has entirely ceased in this walled-off cavity. The abscess cavity is by no means regular in its outline, but it is rather characteristic for it to extend between the muscles and fascia surrounding the joint, forming pockets which are difficult of access; frequently the burrowing of such an abscess extends for quite a distance from the original seat of disease.

Hip disease is primarily a disease of the bony tissue of the joint and abscess occurring in its course is simply an incident, yet one of sufficient frequency to become of great moment in the prognosis of the disease. It may be said that in fully 50 per cent. of the cases of hip disease abscess becomes a symptom of greater or lesser importance at some time or other in its course, and many of the remainder of the cases undoubtedly present deeply situated and circumscribed collections of tuberculous fluid which remain unrecognized and quiescent and disappear under well managed protective treatment. It is also pretty well established that increase in the size of a tuberculous abscess does not necessarily mean an extension of the bone disease and that the retention of the sterile pus does not retard the process of repair of the bone and joint lesion.

Infection with Pyogenic Organisms.—The mortality of hip disease is due almost entirely to the immediate or remote effects of abscess, and it is generally conceded that in the majority of cases it is its infection with pyogenic organisms that constitutes the principal danger. Only in a small number of cases does an abscess become infected before a communication with the exterior is established, but after a sinus is formed either as the result of spontaneous evacuation or of surgical interference it is only a question of a comparatively short time before mixed infection results, no matter what care and precaution is exercised in preventing such an issue.

Orthopædic surgeons agree that in the great majority of cases

the so-called cold abscess is practically harmless in its effects upon the local disease and the general condition of the patient so long as it remains sterile, i.e., uncomplicated by infection with pyogenic organisms. The presence of even a comparatively large collection of sterile tuberculous pus is as a rule unaccompanied by constitutional symptoms of infection.

However, the clinical picture of a case soon changes after infection with pyogenic organisms. The patient soon exhibits evidences of systemic absorption of the toxic products of suppuration in fever of a septic type, in progressive and rapid loss of weight and strength; sooner or later amyloid changes develop as a direct result of the suppurative process, and frequently there occurs a dissemination of the tuberculous disease to such vital structures as the lungs and the meninges. In any case after mixed infection has occurred the ultimate outcome of the disease is doubtful, and in the majority of cases the prognosis is bad. Such a condition of affairs is all the more to be deplored when we consider that the train of symptoms referred to is not at all an indication of the severity of the bone disease, nor is it the result of wide-spread extension of the local process. It has been shown that the tuberculous bone lesion may go on to partial repair while the health and strength of the patient are gradually waning as a result of the suppurative process.

It is then infection of a sterile abscess with pyogenic organisms after a communication with the interior is established which constitutes the principal danger of this complication of hip disease, and for this reason any measures of treatment which do not minimize but which rather invite this danger are to be condemned.

Prompt Evacuation.—Taking up the question of prompt evacuation as soon as a tuberculous abscess becomes palpable we find that the claim for this radical procedure is based, principally, upon the prevention of the danger from infection and of wide-spread burrowing of the abscess before a sinus has formed. Infection before an opening has formed occurs in only such a small percentage of cases that it may be disregarded in establishing a ready rule in the treatment of these abscesses. On the other hand, the danger from infection of the sterile tuberculous abscess as a result of operative interference is real and, to say the least, just as frequent as when a sinus has formed as a result of spontaneous evacuation. Gibney

says: "The operative surgeon is often inclined to resort to a free incision with the knife, and to complete eradication of the abscess with scissors and spoon, believing that he will be able to avoid the danger of infection in the subsequent dressings. Nevertheless no matter how careful he may be the wound sometimes leaks, the sac refills and ultimately there develops a sinus which takes a long time in healing." And Whitman in speaking of the claims of those who would operate says: "Little could be said against this latter course were it not that infection is as common after operative treatment as when a spontaneous opening forms," and again in regard to the danger of extensive burrowing: "The only advantage in favor of the artificial opening is that the cavity with which it communicates should be smaller and more direct than when the fluid has undermined the tissues in various directions, but this is offset by the fact that at least 20 per cent. of the abscesses disappear without treatment." If the abscess were the main feature of the disease or the retention of the sterile pus were inimical to the process of repair prompt incision and evacuation would be permissible, but we know that the abscess is only a symptom of the hip disease, and that there are many cases in which even considerable collections of pus remain quiescent and disappear without impeding the progress towards recovery, and undoubtedly the same thing happens in quite a number of cases which are said to be free from abscess.

Prompt operative procedures cannot be justified on the ground of the relief of the pain, frequently of great severity, often accompanying the formation and burrowing of an abscess before rupture of the capsule. The pain frequently subsides upon incision and evacuation of the pus, but it must not be overlooked that this is due to the relief from the tension within the capsule, and not to the removal of the pus *per se*. Effective mechanical treatment of the joint disease will not only allay the pain, but frequently averts the extension of the abscess and favors its absorption. And furthermore, in the majority of cases when the abscess becomes easily palpable its most painful stage is past. Finally, with the best technic and most cautious antisepsis we gain nothing as far as the progress towards recovery of the bone lesion is concerned by simply evacuating the contents or even curetting the wall of the abscess.

Thus we have so far no rational explanation of the advantages

to be derived from indiscriminate operative interference, and prompt evacuation of abscesses in hip disease as soon as they become palpable must be considered as unsound and dangerous for the following reasons briefly restated: a considerable number of abscesses remain quiescent and become absorbed; retention of the caseous and fluid material does not impede the progress of repair of the bone lesion, nor does evacuation of the pus in any way promote the progress of the disease towards recovery; the sterile abscess as a symptom of hip disease does not constitute a grave danger in well managed cases, except in such a small proportion of cases that they may be disregarded in advocating a dogmatic line of treatment; infection of the tuberculous lesion with pyogenic organisms, if not increased by operative measures, is just as frequent as after spontaneous evacuation; and finally, the recognition of an abscess, unless of such size as to be obvious to the least experienced, depends altogether upon the skill of the individual surgeon.

Absolute Non-interference and Operation upon Definite Indications.—As against prompt incision we have the other extreme of absolute non-interference. Although this can by no means be applicable to all cases and therefore cannot be accepted as an incontrovertible rule of treatment, it appears in comparison with indiscriminate operation as a more rational mode of procedure. When we consider that the abscess may disappear spontaneously, that operation has no effect upon the disease of which the abscess is only a symptom, and, most important of all, that the risk of mixed infection is too grave to be invited by indiscriminate operation, we are forced to the conclusion that letting the abscess alone will probably in the majority of cases give better results than incising it as soon as it is diagnosed.

Operative interference upon certain definite indications as the middle course between the two extremes referred to above is within certain limitations the ideal and most conservative surgical treatment of abscess in hip disease. Clear indications which permit of operative interference are few and, it is true, depend to a great extent upon individual interpretation of the symptoms which may make such a step advisable, but if we adopt the most cautious conservatism against this complication of hip disease we will in the end gain more than by adhering to some one indiscriminate rule of treatment.

Efficient protective treatment of the joint disease will in many cases avert the formation of an abscess, and the same care after an abscess has begun to form will often favor its disappearance. The treatment of the abscess should be, primarily, the treatment of the underlying bone disease. Perfect fixation, rest in bed with extension combined with diet and good hygiene is after all the best surgical treatment of abscess in hip disease. When there appear evidences of infection in the usual local and general symptoms of a septic abscess then recourse may be had to the knife; when, in spite of the most efficient protective treatment, absorption seems unlikely, when the abscess is increasing in size and it is only a question of a short time before it will break spontaneously, when by its size and location it interferes with effective mechanical treatment, then and then only is incision justifiable. We should never lose sight of the fact that abscess is only an incident in the course of hip disease, and that even successful surgical interference has practically no effect upon the prognosis of the bone disease.

Technic of Operation.—If we inquire into the treatment of the abscess after incision of the overlying tissues we again find opinion divided as to the technic to be followed. The various methods advocated and in vogue may be summarized as follows:

1. Non-interference by active measures with the abscess wall followed by drainage of the abscess cavity.
2. Thorough curetting of the abscess wall with subsequent drainage of the cavity.
3. Thorough curetting of the wall and closure of the wound by deep and superficial sutures.
4. Excision of the sac entire and closure of the wound.

Thus we see that opinion is divided between non-interference with the abscess wall and measures to eradicate it as thoroughly as possible, between drainage and tight closure of the wound.

First in regard to the abscess wall, we know that it is the active portion of the abscess, contains the tubercle bacilli and thereby extends to the surrounding tissues by direct invasion. It is probable that the tuberculous process is not confined to the abscess wall, but extends into the surrounding tissues. The successful removal of this granulation wall would be a very desirable step towards the cure of the abscess and complete excision of the sac entire with

subsequent tight closure of the wound the ideal form of treatment. In view of the pathological anatomy of these abscesses such a course is applicable only to a limited number of cases, and is hardly ever accomplished successfully. Curettage of the abscess wall is but a feeble attempt to accomplish the same object. Through a small or even a moderately large incision it is practically impossible in most cases to gain access to all the pockets and recesses of the abscess cavity. And furthermore even if the removal of the abscess wall were complete and successful it would be no security against the formation of another abscess in another locality or against the refilling of the old abscess cavity. As repeatedly stated, as long as the condition which gives rise to the formation of the abscess remains unchanged any measures applied to the abscess itself must of necessity be futile. These unsuccessful attempts to eradicate the abscess wall probably do more harm than good. By injury of the healthy tissue surrounding the granulation zone we weaken its resistance to the spread of the infection, and favor the direct extension of the tuberculous process. The number of cases of acute pulmonary tuberculosis and tuberculous meningitis following incision of abscesses with curettage of their walls would substantiate the belief that breaking up of the abscess wall leads to dissemination of the tubercle bacilli to the lungs and the meninges. As a matter of fact good reasons, based upon pathological facts, are entirely wanting for this part of the technic. Curettage of the abscess wall, as a means of furthering the cure of the abscess, is, to say the least, of doubtful value, and on account of the danger of disseminating the tuberculous infection should not be resorted to.

Closure of the wound leads to union by first intention in a considerable number of cases, but only in rare instances does this healing remain permanent. Breaking down generally occurs as a result of the invasion of the skin by the tuberculous process and of tension from refilling of the abscess cavity. Although it is worth while trying to obtain primary union it does not constitute an important step in the cure of the abscess, and too much must not be expected from it. The same objections that are raised against immediate drainage are applicable to by far the greater majority of cases in which the wound is closed by suture. As a result of the almost invariable breaking down of the incision infection and

formation of long discharging sinuses, at least, are as common in one case as in the other. If it be true that abscess appears only in the more severe cases of hip disease, it would appear rational to believe that drainage is likely to be of benefit to the underlying disease.

Summary of Cases.—A few general remarks as to the nature of the cases reported in this paper are, I believe, of some importance. The series embraces cases of hip disease of varying duration and severity admitted to the Hospital for Ruptured and Crippled, New York, because of pain and deformity. A minority of the cases presented abscess on admission, and only such as from the history and physical examination showed no evidences of previous operation or sinuses are reported. In all cases the patients were thoroughly prepared for an aseptic operation. The operation itself consisted, with minor variations, in strict asepsis, in a small incision, evacuation of the pus, curettage of the abscess wall, drying of the cavity by sterile iodoform or plain gauze, and closure of the wound by deep, buried, and skin sutures. The wound was dressed with sterile, dry gauze and a plaster spica applied to the limbs. In many cases examination of the pus revealed no organisms and in only a few cases were tubercle bacilli discovered microscopically. The amount of pus evacuated varied, but in most cases palpation did not disclose such amounts that spontaneous evacuation was imminent. Most of the cases were under the observation of the writer at the time of operation or subsequent to it, and he feels greatly indebted to Dr. V. P. Gibney for his permission to report them.

A summary of the cases will be found in the table, next page.

Of the thirty-five cases reported the incision broke down in twenty-five at periods after operation varying from one week to three months, except in one case in which it broke down in three days. In one case the incision broke down at an unknown period after operation, and in another case the fate of the incision is unknown.

Eight cases healed by primary union and remained closed one and one-quarter years after operation in one case, one and one-half years after operation in another case, and in six cases for periods varying from one week to four months. In the latter cases no further history was obtained. Out of the remaining twenty-seven

TREATMENT OF ABSCESS IN HIP DISEASE.

Case No.	History No.	Sex.	Hip.	Duration of disease at operation.	Age at operation.	Sinus developed.	Secondary operations.	Results.
1	2696	M.	Double	3 years	6½ years	2 months after operation	Yes	Death from exhaustion 5 months after operation.
2	2680	M.	Left	3½ years	5½ years	8 months after operation	No	6 months after operation sinus still discharging. General health poor.
3	2629	M.	Right	1 year	6 years	?	No	Developed tuberculous meningitis 2 months after operation. Removed from hospital before death.
4	2612	M.	Left	2 years	6 years	Healed by P. U. and remained closed 1½ years after operation.
5	2670	F.	Right	9 months	8½ years	2 weeks after operation	No	Death from tuberculous meningitis 2 months after operation.
6	2708	M.	Right	1 year	4 years	1 week after operation	Yes	Healed after discharging for about 2 years. Two sinuses discharging 1 year after secondary operation. General health poor.
7	2767	M.	Right	1 year	8½ years	Healed by P. U. and remained healed 1½ years after operation.
8	2801	M.	Right	6 months	6 years	2 months after operation	Yes	Death from tuberculous meningitis 1 year after first and 4 months after last operation.
9	3010	F.	Left	1 year	6 years	?	Yes	Sinus healed after discharging for about 1 year. General condition fair.
10	3096	F.	Right	2½ years	7½ years	2½ months after operation	Yes	Discharging sinus 1 year after operation. General health poor.
11	3160	M.	Right	6 months	4 years	2½ months after operation	Yes	Sinus discharging 1½ years after first operation. Septic temperature. Amyloid disease. General condition very poor.
12	3162	M.	Right	1½ years	8 years	3 weeks after operation	Yes	Discharging sinus 1½ years after operation. General health good.
13	?	M.	Left	2 years	12½ years	7 weeks after operation	No	Discharging sinus 1 year after operation. General health fair.
14	3302	M.	Right	6 months	7 years	5 weeks after operation	Yes	Discharging sinus 1½ years after operation. General health fair.
15	?	F.	Left	2 years	8 years	2 weeks after operation	No	Sinus healed 8 months after operation, and remained healed 14 months after operation.
16	3345	F.	Left	?	8 years	Remained healed by P. U. 1 month after operation. No further history.

17	3852	F.	Left	1 year	4 years	Remained healed by P. U. 1 week after operation. No further history.
18	3856	F.	Right	1 year	16 years	Remained healed by P. U. 2 months after operation. No further history.
19	3886	F.	Left	16 years	17 years	Remained healed by P. U. 1 month after operation. No further history.
20	3402	M.	Left	?	10 years	1 month after operation	Sinus discharged for a considerable time but healed about 1½ years after operation.
21	3667	F.	Right	1½ years	6½ years	2 weeks after operation	Rapid decline in health. Death from miliary tuberculosis 2 months after operation.
22	3625	M.	Left	3 years	7 years	2 weeks after operation	Death from tuberculous meningitis 2 months after operation.
23	3698	M.	Left	1 year	9 years	3 days after operation	Ligation of femoral artery	Death 1 month after operation from exhaustion, following hemorrhage from erosion of femoral artery and pneumonia.
24	?	M.	Left	1½ years	4 years	3 months after operation	Discharging sinus 4 months after operation.
25	?	M.	Left	9 months	3 years	3 weeks after operation	Yes	Sinus discharging 1½ years after operation. General health poor. Amyloid disease. Anemia marked.
26	?	F.	Right	1 month	9 years	1 week after operation	Discharging sinus 1½ years after operation. General health fair.
27	?	F.	Right	2½ years	5½ years	3 months after operation	Discharging sinus 3 months after operation. General health fair.
28	?	M.	Left	6 years	8½ years	Remained healed by P. U. 2 months after operation.
29	?	F.	Double	3 years	8½ years	2 months after operation	Yes	Discharging sinus 1 year after operation. General health poor.
30	?	F.	Double	2 years	7 years	2 weeks after operation	Discharging sinus 2 months after operation.
31	?	F.	Right	2 years	5 years	7 weeks after operation	Sinus healed after discharging 5 months and remained healed 1 year after operation.
32	?	F.	Left	7 months	5½ years	2 months after operation	Discharging sinus 4 months after operation. Septic temperature. General health declining.
33	?	F.	Left	5 years	8 years	2 months after operation	Discharging sinus 6 months after operation. Septic temperature. Amyloid disease and anemia.
34	?	F.	Double	2 years	7 years	Remained healed by P. U. 4 months after operation.
35	?	M.	Right	1 year	7 years	5 weeks after operation	Discharging sinus 4 months after operation.

cases there were six deaths: three from tuberculous meningitis, one from acute miliary tuberculosis, one from exhaustion due to suppuration and one from exhaustion and pneumonia following hemorrhages from erosion of femoral artery. One case developed tuberculous meningitis and was removed from the hospital in a hopeless condition. Twenty cases were examined at periods varying from two months to one year and a half, and in fifteen there were discharging sinuses in the line of the incision. In the five remaining cases the sinus formed at the site of operation discharged for varying periods, but finally healed.

The general condition of the patients operated on in whom there has been long continued suppuration is bad in most cases. In at least three cases there were distinct evidences of amyloid changes and many were running septic temperatures with declining health.

CONCLUSIONS

1. The prompt evacuation of abscesses in hip disease as soon as they become palpable does not rest upon a rational foundation, and should not be resorted to.
2. Absolute non-interference cannot be accepted as an invariable rule of treatment.
3. The formation and extension of abscess can be averted in a large proportion of cases by effective protective treatment of the joint disease.
4. The treatment of the sterile abscess as a complication of hip disease should be principally expectant, and should consist in fixation of the joint, rest in bed with extension, tonic drugs, diet and good hygiene.
5. Operative interference may be resorted to under certain circumstances, but must not be regarded as a curative procedure for either the abscess or the underlying disease, and is usually followed by mixed infection.
6. Interference with the abscess wall should be avoided on account of the danger of disseminating the tuberculous process, and therefore operation should consist simply of incision and evacuation of the pus.
7. Closure of the wound by suture may be attempted, but permanent primary union is not obtained as a rule, and in the

majority of cases it is probable that drainage would be beneficial to the bone disease.

8. Mixed infection should be guarded against by more scrupulous asepsis at operation and precautions in the after treatment.

The surgical treatment of abscess in hip disease is by no means a well-settled subject, and no attempt has been made in this paper to lay down definite rules for operative interference. The principal aim has been to point out the error of adopting a dogmatic line of treatment and to make a plea for a more conservative attitude towards this most important complication of hip disease. "Be bolde, be bolde, but be not too bolde," should be the watchword.

Gynæcology and Obstetrics

KRAUROSIS VULVÆ

WITH A REPORT OF TWO CASES *

BY RICHARD F. WOODS, A.M., M.D.

IN studying the literature of kraurosis vulvæ, one is impressed with the great confusion that exists in regard to the term.

As is generally the case when there is ascribed to a symptom the dignity of a distinct entity, there is a failure definitely and properly to understand what the condition really is and what cases should be included under its heading. Thus kraurosis and leucoplacia are described by some as distinct diseases, by others they are considered different varieties of the same condition, and by still others as a syphilitic lesion or stages of senile atrophy; while the almost endless subdivisions that have been made, all depending for their existence on certain well-defined symptoms, leave us in a bewildered state and cause us to wonder what really is meant by kraurosis vulvæ.

In order to get a clear light on this subject, it would perhaps be wise to go back and consider the history of kraurosis, examine the descriptions of this affection by those who first called attention to its peculiarities, and briefly review its pathology, clinical appearance, and symptoms.

Weir was the first to describe this condition. It was in 1875, in an article entitled "Ichthyosis of the Tongue and Vulva," that he described a case which would at the present day be classed under kraurosis or leucoplacia. The patient finally died of an epithelioma developing on the kraurotic area.

In 1879, Lawson Tait described a condition under the title "Serpiginous Vascular Degeneration of the Nymphæ whose Main Characteristics Liken it to Kraurosis."

* Read before the Philadelphia Obstetrical Society, January 7, 1909.

It remained, however, for Breisky to coin a term which described the main symptom of cutaneous atrophy of the vulva, and which has been claimed by many to be a distinct disease. Breisky took the term from the Greek word *κραιῶσις*, "retraction" or "atrophy," and in that word is embodied the chief characteristics of this disease. In his article published in 1885 he says: "In order that the nature of this particular atrophy of the vulva should be more carefully studied, I give it a name which expresses the most clinically characteristic symptom. It is in this sense that I suggest *kraurosis vulvæ*." In his description of this atrophy, he claims "that it merits clinical dignity because it mars confinement and coition."

In following Breisky closely we find that his description of this condition is, however, too extensive. It is too inclusive and too broad in its arrangement of symptoms to be classified under the restricted term of *kraurosis*, for in his description (giving as careful attention to the color characteristics as to the atrophic changes) we have an excellent picture of *leucoplacia*.

I agree with Jayle, who has written a most thorough and excellent article on this subject, when he says in connection with Breisky's observations and description, that he (Breisky) "has taken the part for the whole, a frequent error in science, and that he has doubled the capital pathognomonic symptom which has a nominal value, the atrophic retraction, with an accessory inconstant symptom having only a qualifying value, the color of the skin."

In other words, Breisky described two or three conditions of the vulva, which may occur separately or conjointly, and arranged them under one term; and thus in the literature, as the term is not definite enough, we find all varieties of chronic vulvitis classed as *kraurosis*.

I do not think from a review of the literature on this subject, and a study of the two cases that I report, that we should class *kraurosis* as a distinct disease. It is merely a symptom of a condition of the vulva which fails entirely to describe the whole condition. Nor do I think that *leucoplacia* should be described as a distinct disease. It seems to me that they are all varieties and stages of the same condition, that of chronic vulvitis. These conditions should therefore, according to my opinion, be classified as

varieties of chronic vulvitis: Kraurosis, leucoplacia, pruritus vulvæ.

In order to appreciate the reason for this theory, let us turn for a moment to the consideration of the pathology and the clinical appearance of kraurosis. In regard to the pathology of kraurosis vulvæ, microscopic examinations of Breisky's cases by Fischel showed that the rete Malpighii was contracted, the connective tissue was sclerotic and infiltrated with small cells, the number of sebaceous glands was diminished, the papillæ became contracted, and skin glands were missing in advanced cases; no changes could be discovered in the nerves. Orthman found in addition that there was a thickening of the horny layer, rete Malpighii, and papillæ, and a small-cell infiltration of papillæ and corium. Longyear believes that the pathological changes begin with fibrous-tissue formation, the changes in the skin which follow being the result of this increasing condition of fibrous degeneration underlying these structures, and that this new formation by continuous contraction results in the constriction of the vulva and the strangulation of blood-vessels. Sanger, from a pathological point of view, thinks that kraurosis is "a progressive presenile or senile atrophy of the vulva with pachydermia." Peter regards kraurosis as a chronic inflammatory hypertrophy of the connective tissue with a tendency towards cicatricial atrophy, inflammatory condition of the upper corium layers and epidermis, and degeneration of the elastic tissue. V. Weiss thinks that the pathological process is of the character of a chronic inflammation and that it involves exclusively the upper layers of the corium; while Allegrini considers kraurosis an essential disease in which the "plasmic cells" take the most important part.

We can easily see from these histological descriptions of kraurosis, that no matter how we may look at this condition from a clinical point of view, the lesions are certainly not distinctive to kraurosis, but occur in varying forms in other vulvar diseases.

In 1908, Trespe published a treatise on the pathology of sixty-seven cases, and came to the conclusion that many cases published as kraurosis present the clinical but not the histological characteristics.

Jung concludes, after describing four cases of pruritus, that histologically between a well-marked case of kraurosis and a chronic

vulvitis there exists no qualitative difference, only a quantitative, and that an absolute demarcation should not be established between these two affections; kraurosis should be regarded as the terminal stage of chronic vulvitis. Hence as a distinct malady it should not enter into the nosologic class of affections of the vulva.

It seems that where there is so much confusion in pathological finding, as there is in this disease, it cannot be a very definite condition; thus Mars, Numan, and Heller find the layers of the epidermis hypertrophied, while Orthman, Fischel, Peter, and Young say that the process is one of degeneration and retraction.

The clinical symptoms of this affection are principally those which we recognize in pruritus vulvæ—itching, excoriating discharge, burning of the vulva, especially when in contact with the urine, impairment of locomotion, vaginal stenosis interfering with coitus and labor, and sometimes bladder disturbances.

Let us for a moment consider, in regard to their clinical appearances, kraurosis and leucoplacia. As I have before observed, I believe them to be different varieties of the same condition. Those who regard leucoplacia and kraurosis, however, as distinct diseases, give us in a general way the following distinct clinical differences:

Kraurosis.—Atrophy of skin and mucous covering of vulva; atrophy of labia majora; atrophy and obliteration of labia minora; atrophy of clitoris and vestibule; stenosis of vaginal orifice; on opening the labia, small red-brown spots can be seen on the mucous membrane around the vaginal orifice. Histologically, this disease is a lesion of the derm.

Leucoplacia.—White pearly coin-shaped plaques in the mucous membrane of the labia minora and majora or vestibule, irregular or regular, yellow, white, or grey in color; these cannot be separated by scraping. Clitoris and the labia are atrophied and there is atresia of the vagina. Histologically, this is a lesion of the epidermis.

We can easily see from these descriptions, each taken from actual cases, how much kraurosis and leucoplacia simulate each other and how confusing it is to try to separate them into two distinct diseases.

There are some who claim that kraurosis is nothing more or less than a form of senile atrophy. There is no question, however, in

regard to the difference between them, for while in senile atrophy we have no disappearance of the labia minora, in kraurosis this is the most prominent symptom; also, microscopically, in senile atrophy there is no disappearance of the glands and nerves such as we have in kraurosis. Senile atrophy, the physiological termination of the genitalia, is a far different condition from the pathological state of kraurosis.

There is a peculiar condition following castration in women which causes stenosis of the vagina and changes in the labia and skin, that resemble kraurosis in some particulars. The symptoms of this postoperative vulvitis and atrophy, however, do not compare in severity in the majority of cases with those of kraurosis.

The pathology of this condition is not of especial interest or individuality. There is evidence of slowly progressive fibrosis and doubling of the horny layer, proliferation of the epithelial cells, and the exudation of leucocytes, depending on the degree of irritation. A persistent, excoriating discharge generally accompanies this condition.

In regard to the etiology of kraurosis, there has been much diversity of opinion, as can be seen by the following, all of which have been ascribed by different observers as the cause.

There have been some authors, among them Gaucher, Louste, and Landouzy, who claim that kraurosis and leucoplacia are of syphilitic origin. This theory is hard to prove. The early histories of many cases, it is true, show a specific infection, and kraurosis even occurs conjointly with syphilitic lesions in some cases; but there does not seem to be, from a pathological or clinical standpoint, any conclusive arguments in favor of this belief.

Irritation of various kinds, especially from pruritus vulvæ, masturbation, syphilis, postoperative lacerations of the perineum, reflex origin through defective nerve origin, rheumatism, pregnancy, and gonorrhœa, all have been ascribed as the cause. Most of these so-called causes, however, are merely complications of kraurosis, for how many times do we observe them all, and how seldom the kraurotic condition!

Longyear does not think it a result of a constitutional affection, but a mixed process due to a defective nerve action of reflex origin.

I am of the same opinion as Reed, that the peripheral trophic

nerves or their ganglia are to be considered as the origin of the three varieties of vulvitis, namely, kraurosis, leucoplacia, and pruritus vulvæ. I do not think there is much question, also, but that these three conditions have connection in some manner with the nerve supply of the ovaries or their functioning qualities, as is shown by the changes that take place in the vulva after castration; but if this be true, the question one naturally asks is, why do not more old women suffer from the so-called kraurosis in the same proportion as do the castrated ones. Jayle attempts to answer this question in the following manner: "As a general rule, after the menopause, ovaries do not atrophy with every woman but continue to functionate totally or partially as regards internal secretion despite cessation of monthly epochs."

In its association with cancer lies the importance of this vulvar affection, for there is no question that this condition, regard it as you will, either as a symptom or as a distinct entity, does predispose to epithelioma. In this connection lies the importance of recognizing kraurosis and carefully attending to it. Martin, I believe, was the first to appreciate this fact. He thought that the cells in the hypertrophic area might not atrophy but, increasing in number, might turn the condition into a malignant state. To review a few cases of kraurosis shows us how often this complication occurs.

Edgar out of four cases reports that three developed cancer in from two to three years after the onset of kraurosis. Pettit and Pechevin cut a section from a kraurotic area and made a diagnosis of malignancy. Jung collected sixty cases, ten of which developed cancer; and Trespe, in sixty-seven observations, reports six to have developed epithelioma. In one case of V. Mars's, he found the two conditions co-existing, that is, the epithelioma had developed in the vagina independently of the kraurotic area on the vulva; while in one of my cases, epithelioma developed on the kraurotic area and was the cause of death. Bender makes the observation in this connection that it is the leucoplaxic form that predisposes to cancer, much more so than the kraurotic. However this may be, there seems so much doubt as to what is kraurosis and what is leucoplacia, and there is so much confusion in the cases reported under each head, that this question is impossible to answer.

In regard to the plans of treatment of this disease, as is generally

the case where no method is of service, they have been numerous and varied. The following have been suggested: Nitrate of silver in varying solution, mild solutions of cocaine and carbolic acid, tincture of iodine applied twice weekly, normal salt solution, menthol, dilation with Hegar's dilators, X-ray treatment, which when tried by Stover seemed to augment the disease, neutral acetone of lead in glycerin, and injections of laudanum. All these palliative measures may be of service, depending on the individual case. I found that from 20 to 40 grains of nitrate of silver alternating with the following gave the most relief:

R	Zinci oxidi,	3iii;
	Acidi carbolici,	3iss;
	Glycerini,	3ss;
	Aquæ calcis,	3viii.

In all cases, of course, an examination should be made of the urine, and if there is indication of trouble in the bladder or kidneys, special attention should be paid to these organs. Jayle recommends cauterization of all inflamed points with concentrated solution of permanganate applied on a stylet and made to penetrate into the follicular crypts. Syphilitic treatment should of course be instituted in syphilitic subjects.

Taking into consideration the danger of epithelioma developing on a kraurotic area, if, after a fair trial, local treatment is of no avail, and the age of the patient permits, operative procedures should be at once instituted. Schroeder was the first to operate for this condition; he operated on five cases. Baker has had twelve cases, all of which were operated on. He reports a cure in each instance, a remarkable record. Kummert has had five cures in seven cases; Sanger has operated on two cases; Reed has had six cases with four cures; Brothers, one case with improvement; Küstner, three cases; Longyear, three cases; Kelly, twelve cases with nine cures; Ewald, two cases. Hirst, in one case, resected all of the sensory nerves of the pruritic area and the nerve of the dorsum of the clitoris; and in another, the genitocrural, ilio-inguinal, inferior pudendal, and superficial nerves.

From the number of men who have reported cures in this condition following operation, I think the operation entirely justified. The operation is not difficult, and although the danger of recur-

rence may be considerable, as Price suggests, it should be attempted in all cases where other measures fail. The operation consists in dissecting off the skin of the kraurotic area, that is, the area of skin covering the labia majora and minora and the perineum. This denuded area should be thoroughly curetted and the edges drawn together with catgut. Longyear suggests that after the denudation the mucous membrane of the vagina should be loosened, slipped down, and sutured to the skin, after the manner of the Whitehead operation.

FIG. 1.



Drawing from Case I.

The following are two cases of the so-called Breisky's kraurosis vulvæ that I have observed and treated.

CASE I.—Mrs. M., 60 years of age, a patient of Dr. John J. Black of Newcastle, Delaware, married, and had no children, menopause five years ago. She has been troubled with vulvar itching for four or five years with increasing severity, and lately had noticed an ulcerated area which Dr. Black recognized as an epithelioma and for which he advised surgical attention.

The clinical appearance of the vulvar region was as follows: The labia majora were shrunken and covered with a dry white skin; the mons was covered with a scanty growth of hair, while the labia minora seemed to have entirely disappeared; on opening the vulva, which gave a great deal of pain on account of its tightness and

tenseness, the glazed pearly appearance of the mucous membrane punctated with scattered reddish-brown spots was characteristic. It was almost impossible to introduce the finger into the vagina for examination on account of the atresia and the great pain.

On the left labium majus was an ulcerated area, circular in outline, and slightly larger than a quarter; this had a roughened surface and gave every appearance of being an epithelioma. There was a slight enlargement of the left inguinal glands. This patient

FIG. 2.



Drawing from Case II.

received some local antiseptic treatment and then was operated on by me at the Gynæcean Hospital. On account of the glandular involvement it was deemed wise to remove only the epithelial growth. This was done by making an elliptical incision and drawing the edges together with catgut. Dr. Shuman confirmed the diagnosis of epithelioma by the microscope. The wound healed nicely and the irritation of the vulva seemed to have been much benefited. She returned, however, in four months with a hopeless involvement of the inguinal and saphenous regions and died shortly afterward. The drawing was made before the operation (Fig. 1).

CASE II.—The second case, which I saw at the Presbyterian Hospital in the service of Dr. Edward L. Duer, was in a woman of fifty-two years of age, Mrs. L., who had been suffering for many years with an itching of the vulva. Lately it had become so severe and burned her so smartly that she was beside herself and could get no rest either night or day. Indeed, she presented a lamentable appearance; she had lost flesh and strength, was anæmic, and could hardly restrain herself from attacking her vulva with her hands. The clinical appearance, from which I made the appended sketch (Fig. 2), was as follows: The labia majora were reddened and covered with ulcerated areas from the irritation of the scratching; the skin was dry and harsh; the labia minora seemed to have entirely disappeared, only a slight vestige remaining; the clitoris was atrophied; the vulvar orifice was rigid and it was almost impossible to introduce even the little finger into the vagina; around the vulva in a circular zone the skin appeared grey in color and was hard, dry, and cracked; there were a few red-brown spots on the interior of the vulva, but these were not a feature.

She was given a solution of nitrate of silver and a formula of zinc and carbolic acid; these not giving very marked relief, operation was advised and refused. She continued to come to the hospital with varying improvement for two months, attention being paid to her diet and constitution during this time, when she finally left us.

THE DIAGNOSIS OF PELVIC DISEASE IN WOMEN *

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GENTLEMEN: When we are called upon to make a diagnosis in the pelvic diseases of women, we do so not only by examination but by questioning the patient. One of the first questions which we ask concerns pain, for the location of the pain of which the patient complains is of considerable importance to us in making the diagnosis of pelvic disease. Not infrequently if you will notice the woman as she walks into your office, she will have a peculiarity of gait, or carry herself in such a way as to give an idea of just where the pain is located and where you may expect to find the disease. For instance, if the pain is about the ovary on either side, the woman will usually have her hand over the ovarian region. The reason she does this is not to point out to you the location of the pain, but to relieve the pain to a certain extent by slight pressure.

Pain in the ovarian region, especially if due to a tubal or tubo-ovarian abscess, is not of the sharp, lancinating variety that is observed in peritonitis, but is a dull, throbbing pain, and the patient endeavors to relieve the throbbing by pressing upward and inward upon the abdominal wall. Therefore, whenever you see a woman with her hand pressed over the ovarian region supporting the abdomen, there is a strong suspicion that her trouble is located in the tube or ovary.

There is another kind of pain which often assists us in making the diagnosis, viz., a sharp, lancinating pain. This is seen in salpingitis, or localized or general peritonitis, where acute infection has taken place but pus has not yet formed. Under such circumstances the patient does not suffer that dull, throbbing pain which

* Clinical Lecture delivered at the University of Louisville, Medical Department.

accompanies tubo-ovarian abscess; for in acute salpingitis and acute pelvic peritonitis the pain is of a sharp, cutting character. After nature has walled off the abscess, however, or has endeavored to take care of the pus in the tube, then the pain may gradually disappear, or it may become dull and throbbing in character.

Pain in the back is an important symptom of pelvic disease; and as a rule the patient will complain of aching in the back. This feature does not materially aid us in establishing a positive differential diagnosis, because it is almost invariably a concomitant symptom of displaced uterus, endometritis, metritis, etc.; but it is suggestive of some disorder of the generative organs.

This patient, a woman aged thirty-three years, comes to us with the history of having been operated upon by abdominal section about two years ago. My reason for bringing her before you this morning is to illustrate several points. This woman exhibits several of the symptoms of which many complain after abdominal section. Her principal complaint is a more or less constant pain in the abdomen. We understand that she had a double salpingo-oophoritis, and that both tubes and ovaries were extirpated. In the removal of these structures possibly the operator left some raw surfaces. Now, the pertinent question is, what is likely to happen to these raw surfaces? When the tubes and ovaries have been removed, leaving a stump on either side, these raw surfaces come in contact with the intestines. Of course it is easy to understand that the intestines will become adherent to the raw surfaces, and the result will be what we see illustrated in this case, *i.e.*, in the course of a few months she will have more or less constant pain from these adhesions, and sometimes when the bowels are distended, since they are adherent to the stump, there will be tension on the adhesions, and she will complain of a dull throbbing pain.

The question is very naturally asked, what can we do in the way of relief? Unless the patient desires that we undertake another abdominal section and make an effort to break up the adhesions, we cannot do anything in particular now, because the abdomen has been closed following removal of the tubes and ovaries. Of course the time to prevent future troubles of this nature is when the original operation is performed; and I know of no plan by which this can be more successfully accomplished than by taking

a curved needle and fine catgut and whipping the peritoneum over the stump left after the removal of the tubes and ovaries. This procedure properly carried out leaves no raw surface exposed. It is safe to say that if raw surfaces are left, in a certain number of cases there will occur adhesions and future trouble following abdominal section.

This woman says that both tubes and ovaries were removed, but of course she is not positive about this. She complains particularly of pain in the right side, and we are not certain that the right ovary was not left behind. In some instances the operator will open the abdomen, and if a pus-tube is found he will remove this and leave the ovary, provided it does not participate in the disease. In other cases the operator may remove an ovary and leave the tube behind. I believe we should never leave the Fallopian tube if the corresponding ovary is extirpated. As we know, the original infection takes place in the tube; and since this is true, if the ovary be removed, what adequate reason is there for leaving the tube? If the ovary is infected the tube will be found to participate in the process in nine cases out of ten; in other words the tube and not the ovary is the original seat of the trouble. I am a firm believer in surgical conservatism; we should exercise care in preserving all the organs possible; but I can see no adequate reason or excuse for allowing the Fallopian tube to remain in the cavity when the ovary is removed. It may be correct to remove the tube and leave the ovary intact, but the converse is not true.

Of course we must remember that following abdominal section pain, tenderness, and congestion may exist for some time; and this is particularly true if the patient returns to her customary habits of life too quickly and is not careful to avoid those things which might have a tendency to perpetuate the irritation.

In the case before us, as the patient is unwilling at the present time to undergo another abdominal section, we can only try to impress her with the fact that there is nothing serious the matter with her, and in addition we will institute counter-irritation over the right side of the abdomen, principally for its mental effect. In all instances where pain is of such severity that opiates are necessary to induce relief, I would advise another abdominal section at once; and in such cases there will probably be found ad-

hesions between the intestines and the stump where the ovary and tube have been removed.

In further illustration of some of the points mentioned, I may be permitted to review briefly a case or two that I have recently observed in the Louisville City Hospital: A girl was operated upon for salpingo-oophoritis fourteen years ago. She returned to the hospital six weeks ago complaining of pain "in her stomach,"—there was some pain and tenderness in the upper part of her abdomen, continued nausea and vomiting, and constipation. Examination of the stomach-contents was negative. There was no pain in either ovarian region. I advised exploratory operation in order to ascertain what the trouble was. A small incision was made near the original wound, and passing my finger up underneath the peritoneum the omentum was found adherent over two-thirds the extent of the old scar. That is one of the conditions which will sometimes follow abdominal section, especially where infection was present at the time of operation. The way to avoid it has already been mentioned, *i.e.*, be careful to leave no raw surface exposed within the abdomen, be certain that it is all properly covered by whipping over the peritoneum. In this case it was necessary to dissect off the adherent omentum, break up some few adhesive bands, and the patient left the hospital completely relieved.

Shortly afterward there was admitted to the hospital a woman who had a ventral hernia following abdominal section performed several years before. There was considerable retraction of the scar, and a bulging mass could be readily outlined. The patient was unable to do any work, nor could she walk without discomfort. When the abdomen was opened I found a coil of intestine firmly adherent to the upper part of the original incision. She had suffered some pain in the abdomen, but the symptoms were not especially indicative of the condition found present; still in the course of time she might have had intestinal obstruction because the knuckle of gut might become adherent to the old scar. This is another accident which may follow abdominal section. The intestine was carefully dissected off, and the necessary repair made to the abdominal wall.

The next patient, a woman aged twenty-nine years, married, applies to us for treatment with the history of irregular menstru-

ation, accompanied by considerable pain, and she says there appears to be a tumor in her abdomen. As stated at the outset, before making an examination it is wise to go through the usual preliminary questioning as to her menstrual history, marital history, etc. This has been done, but no facts of especial interest could be elicited.

The first method of examination in all cases of this kind is inspection. We observe the presence of the *lineæ albicantes*, which indicates that the woman has been pregnant. There is an unevenness about the abdomen which is more apparent on the right than the left side, evidently a tumor of some kind exists.

By palpation we will endeavor to outline the different abdominal structures, a procedure which will aid materially in arriving at the diagnosis. We are able to outline an irregular mass or tumor extending toward the right side from the median line; the growth is hard in consistency and especially prominent at its upper margin. It is observed that this tumor does not move with either inspiration or expiration. We can feel some evidence of pulsation in the enlargement. The patient says the presence of this growth in the abdomen was first noted three or four years ago.

By percussion it is hoped we may be able to determine whether this tumor is solid, liquid, or composed of gas. Our conclusion is that the growth is a solid mass, there is no evidence of fluctuation and we have excluded a gaseous tumor. No additional information could be gained by measurement in this case, the presence of the abnormal growth is apparent by even casual inspection.

We now come to the question of digital examination, but we have passed some of the history that perhaps should be mentioned, viz., the patient states she is the mother of one child, now three years old, and that she has had three miscarriages.

We will omit at first critical examination of the external genitalia, as the point it is desired to determine is whether or not the tumor mentioned is connected with the uterus. We want to know first whether the uterus moves with the tumor, and whether we can get the fingers between the fundus uteri and the tumor. This will be determined by the method known as bimanual examination. Possibly in this case we may be able to make an accurate diagnosis without the administration of an anæsthetic. Regarding the mis-

carriages, it is unknown whether they were criminally induced or otherwise, nor is it known whether she had any particular trouble after any of them.

Examination discloses the fact that the patient's abdomen is very tender. The uterus is found in its normal position of slight ante flexion, the cervix is not patulous. I will now endeavor to outline the uterus. I have my finger against the cervix, and by pressing upward thereon it is found that both the uterus and the tumor move, *i.e.*, we find that the tumor moves with the uterus. Tenderness is most marked on the right side, there is a mass in the right posterior *cul de sac*, and another smaller mass on the left side of the uterus. From the examination thus far the uterus feels like a fibroid, and I can detect a nodule on the posterior wall.

In all probability this condition has been present for some time, there being a mass in the posterior *cul de sac* on either side. Originally she may have had an infection in the tube, or about the tube and ovary, but nature has taken care of the abscess; it has been walled off and pus has been prevented from entering the general cavity by protective adhesions; and if there is now any pus present in the Fallopian tubes it is in all probability sterile. It is likely, however, that nature has taken care of the pus originally present, that the fimbriae of the tubes have become obliterated, and that the tubes and ovaries are embedded in a mass of adhesions. I would say that originally this woman had acute salpingitis followed by pyosalpinx, that the infected area has been walled off by nature, and as a result the structures involved are now bound down by a mass of inflammatory adhesions.

As to the larger tumor demonstrated present on the right side, I am unable to make a satisfactory diagnosis without an anæsthetic. The growth seems to be in the broad ligament; and there appears to be a mass on the posterior wall of the uterus, probably a fibroid.

Remember that a satisfactory bimanual examination cannot be made with the patient lying on the side; she must lie on her back, and you should ask her to raise up off her hips, resting her weight on the shoulders and feet. This throws the cervix upward and gives you a free field in the posterior *cul de sac*, allowing you to determine easily if there is any abnormality or tumor present there.

This tumor on the right side may possibly be an old inflam-

matory mass. It may be a tubo-ovarian abscess, it may be an ovarian cystoma, it may be a fibroid attached to the uterus by a long pedicle. We can only speculate as to its actual character from the examination we have made. The growth seems to be movable to a limited extent, it extends over to the uterus, but does not appear to be intimately attached to it.

What is to be done in a case of this kind? Certainly no local treatment will afford relief. The only thing we can advise is operative intervention; the abdomen should be opened in order to determine the true condition of affairs, and then the proper treatment may be applied.

I would venture a diagnosis, which may have to be changed when the abdomen is opened, that in this case we have an old tubo-ovarian abscess with possibly a complicating ovarian cystoma on the right side; that infection probably occurred following one of her miscarriages, presumably the last one, as she now says she was in bed for four weeks at that time and had fever. She probably had an acute salpingitis followed by pyosalpinx, which is the usual result in such cases.

The next patient, a colored girl aged eighteen years, comes to the clinic with the history of "sores on her privates," as she terms it. This is a class of cases that we do not care to treat in the gynæcological clinic, but the patient being here we will endeavor at least to make a diagnosis. In private practice one does not encounter a great many cases of venereal disease in women (chancre or chancroid) as extensive as this. But in hospital work many such instances are necessarily observed.

The question for us to decide in this case is, as to whether the sores are specific or non-specific in character. In order to arrive at a decision it is necessary to ascertain if possible when infection took place, *i.e.*, when the patient was exposed or made herself liable to the infection; second, the length of time which intervened between this exposure and appearance of the sore; third, we must note whether the lesion is single or multiple, and the general appearance of the sore. These and numerous other points will aid us in making the diagnosis. It must be remembered that chancre is a hard sore, it is indurated, that it can be picked up so to speak between the thumb and finger, that it imparts a

sensation of cartilaginous hardness to the examining fingers. Now by the use of rubber gloves I will examine this patient more thoroughly. I do not believe in exposing one's self unnecessarily in this class of cases, and if we are compelled to examine them let us "handle them with gloves."

Although this girl is but eighteen years of age, she tells us that she has borne two children. As result of childbirth we find quite an extensive laceration of the perineum, and separating the labia we note several sores which on inspection have the appearance of chancroids. Chancre is usually found as a single sore, while the converse is true with chancroid. Moreover, the base of these sores is not hard as would be true in chancre. The diagnosis is chancroids.

What is to be done in the way of treatment? The principal indication is thorough cauterization, and there is nothing better for this purpose than the application of nitric acid. The actual cautery might be used if an anæsthetic is given, and the result will be just as good. There are several means by which cauterization may be effected, and it may be well to enumerate them: (1) the actual cautery, (2) nitric acid, (3) lunar caustic.

After the parts have been adequately cleansed, and the sores thoroughly cauterized, the vagina should be kept clean by irrigation, in order to promote the healing process. It is questionable whether dusting powders accomplish much good in cases of this kind, although they are in common use. If this patient were in the hospital the vagina could be kept clean by douching twice daily, and the sores could be cauterized whenever necessary to prevent further extension. I could show you several patients in the city hospital where involvement of the labia and vagina was much more extensive than it is in the case before us, in which rapid improvement took place under the plan of treatment outlined. Without adequate treatment the sores in this case would undoubtedly extend until the entire labia would become involved, and there would be a corresponding increase in the inflammation, tenderness, swelling, and discomfort.

As a preliminary treatment we will irrigate the vagina thoroughly and then cauterize the chancroids with nitric acid. Observe that we are careful to have no excess of acid on the applicator,

because we do not wish to do injury to the healthy tissues about the sores. Some physicians prefer to use cocaine locally before applying nitric acid, but the pain produced is usually not sufficiently severe to make this necessary. Especial attention is called to the manner in which the disease has spread in this case; note that there has developed a smaller sore on the right labium directly opposite and in contact with the larger one on the left side. I believe further extension will be prevented by the treatment instituted.

We will instruct this girl to keep the parts clean and dry. That is one of the principal things to be observed, and perhaps she can best do so by the liberal use of a dusting powder composed of stearate of zinc and boric acid following each douche.

Ophthalmology

INTRA-OCULAR TUMORS

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So large a subject must of necessity be treated in one of two ways in such a paper as this. On the one hand, the whole subject may be gone over rapidly, prominence being given to one or two points which are of special importance; or, on the other hand, a special case may be described and from it a series of points selected for elaboration.

In the present instance the former method will be followed, special attention being paid to the subject of the diagnosis in early stages.

Frequency.—On the whole, intra-ocular tumors are of very rare occurrence, as may be judged from the fact that of nearly 250,000 new patients seen at the Glasgow Eye Infirmary in twelve years the percentage of cases of intra-ocular tumor comes to 0.03 per cent. The percentage of cases usually cited is that of Fischer, 0.06 per cent. of cases of eye disease at a public hospital.

CLASSIFICATION.—Intra-ocular tumors are either uveal or retinal in origin, the former being much more common than the latter, in the ratio of nearly 20 to 1.

Uveal tumors may be either malignant or benign, the former alone being considered here, although various benign new growths have been described, as they are very much more frequent than the malignant.

Uveal new growths, then, are either carcinoma, a very rare growth and usually secondary in origin; or sarcoma, which is the ordinary form of uveal malignant neoplasm.

The *carcinoma* is, as remarked above, usually secondary to some other carcinoma, say of the mamma or other part; but occasionally

a carcinoma may be primary, taking origin in the ciliary-body or iris pigment endothelium.

The remarks as to appearances made under the head of sarcomata may be taken to apply to carcinomata of the uveal tract; but the presence of a primary tumor of the breast or other part which is carcinomatous would give rise to suspicion as to the nature of the ocular growth. It is worthy of note that there is a considerable accumulation of evidence with regard to the nature of the chorioidal sarcomata, the view being expressed that such growths may in reality be endothelial in origin, therefore endotheliomata; and there is much to be said for this view.

The *sarcoma* of the uveal tract is usually divided into two classes, pigmented and non-pigmented—the so-called melanosarcoma or melanoma and the leucosarcoma. The line of distinction is by no means clear, as some tumors are black, some grey, and some contain absolutely no pigment. Generally speaking, however, any tumor may be considered to be non-pigmented when it contains only such pigment cells and granules as may be the result of the breaking up of the chorioretinal pigment layers. Pigmented sarcomata are much more common than the non-pigmented (3 to 1).

In other respects, also, uveal sarcomata may be divided into classes according as they form a dome-shaped or a flat mass; or as they are composed of round, spindle, or mixed round and spindle cells. The dome-shaped growth arises from a limited base and tends to grow forward, pushing the retina in front of it and forming, it may be, a pedunculated mass; while the diffuse, flat, or plaque-shaped growth extends its base widely, but attains only a small height. The former are much the more frequent (10 to 1).

Melanomata usually occur in late middle life but may occur in persons under thirty or over seventy years of age. The youngest subject seen was aged 19 years, a girl in whose eye a deeply pigmented, dome-shaped growth was found. Another case was seen in a woman aged 20, in whose eye a diffuse growth was found. In both cases the tumor was composed of mixed spindle and round cells.

Leucosarcomata are tumors of younger persons, often only infants, but are sometimes found in persons of mature years. The character of the growth is, however, quite different, as that found in

children is a round-cell, whilst that of old persons is a spindle-cell growth.

DIAGNOSIS.—Knapp first, in 1868, called attention to the four so-called stages of the clinical history of intra-ocular sarcomata. The *first* stage is that in which the growth is subretinal, giving rise to little or no external sign of inflammatory disturbance. The *second* stage is characterized by increase of intra-ocular tension and its consequences. The *third* stage is that in which the tumor escapes by continuity of tissue from the limits of the sclerotic capsule; and the *fourth* that in which the growth becomes generalized by metastasis.

In the *first stage*, the earliest sign of any affection of the eye is generally dim vision, which may be sharply defined, forming a definite scotoma. This may be accompanied by metamorphopsia (distorted vision), due to uneven elevation of the retina by the thickened underlying chorioid. Examination of the eye is usually called for on account of dimness of sight alone, however; and in this stage an elevation of the retina may be recognized by difference of focus. Fulness of one of the anterior scleral veins due to pressure upon the large veins, or abnormal distention of the same in the eye, an unevenly dilated pupil or unevenly acting ciliary muscle, due to pressure upon one of the ciliary nerves, may be found as corroborative evidence.

The principal and most reliable sign, however, is the elevation of the retina. This is naturally of variable extent and shape, its size and outline being to some degree dependent upon the underlying growth. If the tumor occupies a posterior and central position, the dim vision will be well marked and clearly defined, and the change in position of the retina will be easily recognized. If, on the other hand, the growth be at the anterior part of the globe, no sign or symptoms may be discovered until a later stage.

The appearances of the elevated retina may vary considerably. Sometimes it is almost like normal retina, and only accurate focusing and the watching of the change in the curve of the vessels which pass over it render it distinguishable. At other times it may, if adherent to the tumor, present a bluish color in which traces of the chorioidal vessels may be noticed; or, lastly, if there has been any inflammatory action in the retina, it may be greyish-pink in

color. The margins of such elevations are often sharply defined, at the upper part especially; and there may be a noteworthy amount of pigment deposit there also. The surface of the elevated retina may be smooth or lobulated, but its principal characteristic is its fixity, that is to say, it does not move on rapid movement of the eye as an ordinary separated retina does.

An effusion of fluid may, however, take place over the tumor and give rise to a true floating separation of the retina. Usually this serum gravitates to the lower part of the eye so that ultimately there may be an elevation of the retina at one part and a separation of different appearance at another, the two possibly continuous. Such an effusion may occur somewhat rapidly and give rise to great difficulty in diagnosis, especially when the eye is seen for the first or second time only.

The fixed elevation of the retina must be distinguished from that which occasionally follows injury and is produced by hemorrhage under the retina or chorioid. The red color which is usually found where there has been hemorrhage will generally aid in making the distinction. When there is an association of a fixed and a floating separation of the retina, and especially where the latter overlaps the former, as where the tumor is growing from the lower part of the fundus, the diagnosis is more difficult and various devices have been resorted to to assist the surgeon. If the history does not suffice, if the gradual increase of blindness in a previously healthy (not myopic) eye and the absence of injury, local or general, does not enable the surgeon to come to a conclusion, it has been suggested by Von Graefe that atropine may be instilled, after explanation to the patient of the object, to try to produce a glaucomatous state. Hirschberg advocated puncture of the sclera to draw off the fluid from the floating separation. Fraenkel punctured the sclera with a needle to feel the separation or even to puncture it to feel what was below it. Jackson has, with others, suggested the use of ophthalmoscopic examination, using direct sunlight, which will penetrate an ordinary separation, and possibly reveal the existence of a solid mass below. This leads naturally to transillumination, which has been recently rendered more satisfactory by Würdemann's very excellent lamp. Used in favorable stages there is no doubt that transillumination frequently assists greatly in forming a diag-

nosis, but only a limited area of the eye can be investigated by it. Transillumination from the mouth sometimes assists if the tumor is in the lower part of the eye; but where the separation extends far back it is often very difficult to exclude positively the existence of tumor.

In the early stages, it may be remarked here, the very existence of an elevation of the retina may be missed unless a mydriatic be used, and unfortunately it is just in such a case that one may hesitate to use such a drug.

Second Stage.—In this condition the diagnosis must largely depend upon the previous history of the affection of the eye. No clinical history, however, can be quite definite enough to enable the surgeon positively to affirm that there is a tumor in an eye, although it may give rise to a strong suspicion.

A history of a slowly progressing blindness for six or more months affecting one eye only and terminating in an attack of acute glaucomatous hypertony would justify strong suspicion, especially if the patient were under forty-five years of age, as fulminating glaucoma is very rare before that age. The signs and symptoms of the second stage are those essentially of the acute glaucomatous condition. It is, however, probable that some assistance may be obtained from a study of the nature of the pain experienced. In some cases of secondary glaucoma (from tumor) the pain seems to be more recurrent than continuous, as in glaucoma simplex; but it is by no means always possible to get a history of pain correctly.

Recently I have suggested a point which has proven of assistance in two cases of this nature, namely, that after the opening of an eye for the performance of iridectomy as in an ordinary glaucoma the tension be felt lightly, and if the tension is very distinctly lowered after drainage of fluid the case is likely to be glaucoma; whereas if the tension is not appreciably or notably lowered the case is likely to be either tumor or intra-ocular hemorrhage.

No information is to be gained from the formation of ectasia in the ciliary or equatorial region, as these may occur in chronic glaucomatous states due to various causes, unless the ectasia be punctured, when the nature of the fluid which appears may assist. If the ectasia be opened, however, an opportunity is given of investigating with a probe the state of the interior of the globe; and the

surgeon should be prepared to follow this procedure by excision at once.

Third Stage.—In this stage if a nodule of outgrowth appears at the ciliary margin, its mode of extension and firm consistence will generally assist in establishing the diagnosis. At all events the somewhat rapid growth of such a nodule, taken in conjunction with the past history, will usually serve to confirm a previous suspicion.

It occasionally may happen that a large ciliary staphyloma may be mistaken for a tumor, and the error is more easily made than might be imagined, as such an ectasia may project between the eyelids and hide the cornea completely. A second glance will generally decide the matter, however, as the cornea or its remains is always lifted, as it were, by a staphyloma, whereas it is usually overgrown by a tumor nodule.

If the outgrowth be equatorial it will usually have so hard a feeling that it cannot be mistaken for an ectasia.

In cases where the outgrowth is posterior there may be loss of motility of the eye or proptosis to assist in the diagnosis. In this stage of tumor growth the tension of the eye may be much reduced from the previous state; indeed the eyeball may present a shrunken appearance, and in advanced cases, when the outgrowth is much larger than the original tumor, the eye may become a mere appendage, as it were, of the tumor. Such cases, however, require no special diagnosis as a rule.

It must not be forgotten that the tumor growth may escape from an eye by several different channels and that several outgrowths may be present at the same time.

Fourth Stage.—Generally speaking, the fourth stage of tumor growth is found in general hospitals and often only in the post-mortem room. Occasionally, however, the glands in the neck become involved or the brain cavity is invaded; but usually the secondary growths are found in the liver, skin, or intestines. The presence of melanin in the urine may assist the diagnosis.

Duration of Stages.—The first stage of the growth of an intra-ocular tumor may last from six months to a year, but it must not be forgotten that many things may occur to complicate the history. The tumor may be growing in an eye formerly affected by some other disease, even in an old and shrivelled stump, so the duration

of the stages is a matter of little diagnostic significance except as before mentioned. Further, it may happen that a tumor may become quiescent and lie dormant for some years. The second stage, if uninterfered with, fortunately rarely now but frequently in former years, lasts usually about three months. The third and fourth stages have no time limits, properly speaking. If, however, an eye has been removed on account of a tumor and no secondary growth be manifest, even after microscopical examination of the globe, the patient may be considered to be safe from a recurrence if he lives for three years. If the eye be removed during the third stage and the orbit cleared out and cauterized thoroughly the same may be said. In the fourth stage, of course, there is practically no hope from the first that the patient can survive.

Tumors of the Ciliary Body.—Turning to a brief glance at the special features of cases of sarcoma of the ciliary body, the first point to be noticed is that the posterior part of the fundus will show no change for a long time. As against this, however, the signs of a tumor of the ciliary body may be early noticed, as the pupil may be altered in appearance or the lens may be pushed to one side by the advancing growth. In other cases the pigmented mass may be seen in the pupil or growing through the iris or pectinate ligament into the anterior chamber. In cases of this nature the growth may, though rarely, penetrate the sclerotic fairly early, owing to the vascularity of the tissues. The diagnosis of tumor is more frequently made in the first stage of ciliary growths than of posterior growths, as such special signs as above noted usually show earlier than in the others.

The diagnosis between malignant neoplasm and gumma of the ciliary body is usually established by the existence of inflammatory symptoms in the latter, whereas none are present in the former.

Tumors of the Iris.—In the iris sarcoma is almost always deeply pigmented. It usually begins as a small rusty spot which, unlike those small pigment spots frequently seen in this situation, increases in size. The gradual increase in size and projection into the anterior chambers of a pigmented mass, in the absence of signs of inflammatory changes, would be quite enough to establish the diagnosis of sarcoma. Syphilitic and tubercular nodules are always accompanied by signs of irritation; and the pearly nodule, which is a species of

fibroma, the cyst, which is usually a sequence of injury, and the nævus have appearances which are quite easy to distinguish.

Primary sarcoma of the iris is an exceedingly rare growth, but as above indicated the iris may be involved secondarily by a growth in the ciliary body or chorioid and, in consequence, the posterior part of the eye should always be examined for signs of tumor growth if there is the least reason to suspect its existence as indicated by the appearance of the eye.

LEUCOSARCOMA OF THE CHORIOID.—This is a tumor of earlier age than the melanoma, but, though rarely, may be seen in advanced years. It may be remarked here that the white sarcoma which is seen in adults is practically always a different pathological or histological type of growth from that seen in children. In the adult the growth is a spindle-cell or fibrocellular tumor, whereas in children it is a round-cell growth of much higher malignancy. The growth seems to take origin, as in melanoma, from the external layers of the chorioid in adults, whereas in children its origin is in the internal layers. In adults the diagnostic features do not differ from those of the melanoma.

In leucosarcoma of children there is often confusion between this growth, glioma of the retina, and pseudoglioma; and a few remarks upon this subject may be made here, both from the clinical and the pathological point of view.

Clinical.—As a young child cannot, as a rule, call attention to its subjective symptoms, it is usually only at a comparatively late stage that the existence of the disease is first noticed. Thus, whether the tumor be a leucosarcoma or a glioma, it very generally happens that the first sign observed by the mother is the existence of a white or yellowish-white reflection from behind the pupil. Now, as in either case the cause of this alteration of the appearance of the reflection is separation of the retina, occasionally accompanied by degenerative changes with clouding of the vitreous body, there can be but little distinction between the two growths. In certain cases, where a glioma of the retina is growing from the internal nuclear layer (glioma endophytum), the surface visible with the aid of the ophthalmoscope is rough and the blood-vessels have not the characteristic appearances of those seen in separation of the retina. This fact may serve in a few cases as a distinguishing feature; but

much more commonly the surface of the retina is much as in ordinary separation, only more whitish in color (as in glioma exophytum).

In leucosarcoma of the chorioid the retina is often degenerated in a more or less high degree, and is often pressed tightly forward against the lens so that no blood-vessels can be distinguished in it.

In both glioma and leucosarcoma the tension is elevated comparatively early and the usual results, abolition of the anterior chamber and dilatation of the pupil, are manifest. Often it has been noted that the sclera presents an absolutely clear bluish-white appearance, there being no vascular dilatation on the surface; but this is usually seen in cases where the tension is elevated.

Lastly it may be stated that if both eyes are affected it is much more likely to be leucosarcoma than glioma, as in the writer's experience bilateral (simultaneous) affection is exceedingly rare in glioma.

As regards the distinction between intra-ocular tumor and the so-called pseudoglioma in children, there is usually, but not always, one principal point of difference, namely, the tension, which is very often below normal in pseudoglioma, especially in the later stages. Moreover, the pupil is usually contracted and fixed, the iris being bound to the lens capsule more or less extensively. Pseudoglioma in children is, however, not the result of cyclitis in all cases, and it may be found every now and again that the tension is increased and the pupil dilated whilst no new growth is found on opening the eye. Such cases may be due to simple separation of the retina, and the writer has notes of such a case in which both eyes became affected, all the usual evidences of tumor being present, in a child aged fifteen months; and yet after excision absolutely no sign of tumor was found (no hemorrhage and no evidence of past cyclitis).

Again, tuberculosis of the chorioid in children may give rise to appearances which are exceedingly like those of intra-ocular tumor and the possibility of this should be remembered.

To sum up the consideration of the diagnosis of intra-ocular tumors in children, it must be stated that this is often a matter of great difficulty; and after seeing a considerable number of such cases clinically and making examination of the eyes after excision, the writer has come to the conclusion that it is rarely safe to attempt

to foretell exactly what will be found by the pathologist from the clinical appearances.

Pathological.—Regarding the distinction between glioma and leucosarcoma from a pathological point of view there is still room for considerable investigation.

Glioma is distinctly less frequent than leucosarcoma and is a tumor of earlier age than the latter. There is little difference in the matter of malignancy, as both growths tend to recur early. Glioma usually spreads by way of the optic nerve and its sheath, while leucosarcoma usually spreads by formation of nodules on the sclera, or in it if found early enough. Glioma does not tend to involve the lymph-glands in the neck, but leucosarcoma does.

The histological distinction between the two types of new growth may be considered here for the sake of continuity.

Legrange of Bordeaux was probably the first to dispute the retinal origin of some of the intra-ocular tumors of childhood; and the writer has considered the matter carefully during the last twelve years, when owing to the kindness and courtesy of several of his colleagues he was enabled to see cases clinically as well as pathologically. The conclusion come to was that undoubtedly many cases which appeared to be glioma were really sarcomata taking origin in the chorioid. It is undisputed that, even in such cases, the retina may be involved, by the growth bursting through the lamina of Bruch and so involving the retina secondarily, and many examples of this have been seen; but, on the other hand, it is also undisputed that glioma of the retina may give rise to secondary involvement of the chorioid at the optic nerve entrance by continuity of growth. The latter, in the writer's experience, has been seen only twice.

Generally speaking, the histological appearances of the growths may be identical, although the formation of tubules in the growth is more frequently seen in glioma.

Latency of Chorioidal Tumors.—The term latency is here used to indicate that state of a tumor in which it seems to undergo degenerative changes which for a greater or less length of time prevent its advancing growth.

Many instances of this have been seen and recorded. In some the tumor has undergone fatty degeneration and remains as a clearly defined mass, the component tissue of which is so highly altered that its precise nature is indeterminate. Crystals of fatty

acids are commonly found in the mass, and sometimes crystals of cholesterin are found free in the fluid which usually lies round them. In other cases, whilst a mass of such a kind is found in an eye, it is surrounded by an actively growing tumor, and a point of origin from which the new portion has sprung can easily be recognized.

Such degenerated tumors may be found in children as well as in adults. The period of degeneration may not be of long duration, as in three cases seen by the writer the patient was under two years of age. In one case, of an adult, twenty years had elapsed since the onset of glaucomatous symptoms, and in another six years; but it is uncertain whether the tumor had begun at such early dates.

Regarding the cause of the degeneration it is difficult to say much. Probably the explanation is to be found in blockage of the main supply-vessels during the period of glaucoma. The sharply cut outline which is usually found to be present in such cases seems to support this theory, for were the degeneration the result of rapid tumor growth only the parts more centrally situated would probably degenerate first and a gradual transition would be recognizable.

The explanation of the renewed activity is not very difficult when one takes into consideration the highly vascular nature of the tissue surrounding an intra-ocular growth and the certainty that some of the blood-vessels have been more or less involved in the growth. The condition of matters is somewhat analogous to the occurrence of a secondary growth in the orbit some months after the eye and its contained tumor have been excised.

Secondary Tumors.—Secondary tumors arising from intra-ocular growths may occur in two ways: by metastasis or by continuity of growth, the latter being much the more frequent.

When metastasis occurs the growths are usually found in the abdomen (liver or intestines), but secondary nodules may occur anywhere over the body. Such nodules may or may not repeat the histological characteristics of the primary. In one case of deeply pigmented sarcoma of the chorioid secondary nodules were found, some pigmented and some non-pigmented. Growths occurring by continuity of growth may occur in the orbit, whence the bony cavities surrounding it may be involved and eventually the brain. In a few cases only are secondary growths found to invade the tissues of the face and neck and sometimes the glands in the neck, but this last only very rarely.

Otology

REFRIGERATORY FACIAL PARALYSIS: HOW IS IT PRODUCED?

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It is a curious fact that some of the most common diseases with which we have to deal are the affections least well understood; and, what is perhaps more astounding, this lack of understanding is not infrequently due to ignoring perfectly patent facts rather than to the non-existence of established knowledge. It is not odd that any particular physician should fail to possess full knowledge of any given medical subject; the field of medicine is so broad and the new discoveries, with their consequent alterations of old views, so frequent and rapid, that one mind can scarcely keep track of the entire range. But to witness the great mass of the profession calmly ignoring for years a clearly proven discovery in medicine, one even, perhaps, that makes for ease and certainty in diagnosis and success in treatment, must ever be an astonishing phenomenon. Numerous instances of such conduct might readily be cited, but the subject of this discourse is a sufficiently glaring example.

It is now a matter of many years since neuropathologists abandoned the notion that infantile paralysis and facial palsy were the result of lesions of the nerve-endings in the muscles, and of more than half a century—as long ago as 1857—since the true pathology of refrigeratory facial paralysis was pointed out; yet to-day there is scarcely a single well-known text-book on Neurology or the Practice of Medicine, in the English language, that sets forth the perfectly evident facts relating to the mode of production of the lesion. Indeed it is rather interesting to note the unanimity of

opinion and similarity of expression concerning the etiology, prognosis, and treatment of facial paralysis in the most prominent of these text-books, and to mark the almost complete absence of anything like a satisfactory statement on the pathology of the disease. If you will review such recognized works as Dana's "Text-Book on Nervous Diseases," Starr's "Organic Nervous Diseases," Mayer's Translation of Oppenheim, "Nervous Diseases by American Authors," Clifford Allbutt's "System of Medicine," "The Encyclopædia Medica," the "Practice of Medicine" by Osler, Wood and Fitz, Salinger and Kalteyer, and Adolph Strumpell, you will find that they are agreed upon the percentage of cases supposed to be due to exposure to cold and upon the line of treatment to be followed. With one notable exception, they offer no better explanation of the pathological process involved than might be embodied in the statement that the lesion is a neuritis, resulting from the effect of cold upon the nerve-trunk or its terminals, most of them implying a belief in the theory that the cold produces its destruction by direct action upon the nerve-terminals or the trunk after it emerges from the stylomastoid foramen. All who describe the prodromic symptoms make some reference to the ear, several saying that the palsy is usually preceded by pain in the ear, tinnitus aurium, deafness, and, occasionally, fever and nausea; yet none seem to consider that this reference has any bearing upon the pathology of the disease.

In a paper read before the Johns Hopkins Hospital Medical Society, December 2, 1901, I called attention to what I believed to be a neglected factor in the consideration of facial paralysis; a factor which is of importance not alone as a means of explaining the pathology of the majority of cases of this affection, but of prime importance in determining their proper treatment. In that paper I announced the conviction that "*in the majority of cases, if not indeed in all, of facial paralysis of the 'refrigeratory' or 'rheumatic' class, an acute or subacute otitis media is an intermediary condition between the exposure to cold and the appearance of the paresis.*"¹

A very brief investigation of the literature showed me that while this idea was at variance with the popular text-books it was not entirely new. Berard seems to have been the first to call attention

¹ Johns Hopkins Hospital Bulletin, April, 1902, vol. xiii, p. 83.

to the possible relationship between a subacute otitis media and the paralysis; and Roche was roundly scored by a congress of physicians a year later when in discussing Deleau's paper upon the same subject he had the temerity to suggest that this might be the usual explanation of the occurrence of refrigeratory facial paralysis. In striking contrast to the attitude of English authors, however, is the acceptance of this view by the French and German writers. In France particularly the most authoritative works present, as the most satisfactory obtainable explanation of the production of facial paralysis following exposure to cold, the theory that between the exposure and the supervention of the paralysis there is an otitis media with coincident injury to the nerve where it passes through the tympanum. Charcot, Bouchard, Duplay, Testas, Despaigne, and Lannois may be mentioned as among those in whose books the theory is set forth. Among the prominent German authorities, Baerwinkel² stated forty years ago that "*the disease is always accompanied by an affection of the middle ear; the lighter cases with a serous, quickly absorbable exudation, and the severer forms with a plastic exudation.*" Erb, in Ziemssen's "Handbuch der Spec. Pathologie," and Berger, in a special article on the "Pathology of Rheumatic Facial Paralysis,"³ written more than thirty years ago, give expression to the same views.

Although I have published one rather long paper upon the subject,⁴ a general recognition of the true pathology of refrigeratory facial paralysis is a matter of such great importance that I feel justified in endeavoring again to bring the question to the attention of the profession. Certainly the question does not seem to have received the consideration it deserves. The affection is a serious one, and if neglected or improperly treated means a sad affliction in the shape of a deformity that cannot be hidden; but I believe that in the vast majority of instances the paralytic condition is dependent upon a very simple lesion of the middle ear which will respond satisfactorily to proper treatment if instituted promptly. Let us see what reason there is for this belief and whether we have a sufficient foundation upon which to base the statement that an

² Deutsch. Archiv f. klin. Med., 1867, vol. xiv, p. 122.

³ Deutsch. med. Wochen., Dec. 9, 1876.

⁴ Trans. Amer. Otol. Soc., 1904, p. 364.

otitis media is always an intermediary stage between the primary action of the cold and the terminal paralytic affection.

All of the recent writers upon the subject seem to have accepted the statistics offered by Philip and Heubschmann as presenting a fairly accurate subdivision of the cases of Bell's palsy, according to etiology, *i.e.*, that about 3 per cent. are of syphilitic origin; 5 to 6 per cent. of a traumatic nature; 6 to 9 per cent. due to otitis media; and that from 72 to 75 per cent. are caused by "exposure to cold." This last large group is usually spoken of as the "rheumatic" or "refrigeratory" type. The process of involvement of the nerve in the syphilitic or traumatic cases, and in the otitic cases where necrotic invasion of the Fallopian canal can be directly traced through a chronic suppurative otitis media, is perfectly clear. But what is the nature of the disease process involved in that large collection of cases included under the heading "refrigeratory facial paralysis"? To state simply that a disease is produced by exposure to cold, does not give one a very clear notion of its pathology, nor does the additional declaration that it is rheumatic in character help in the slightest degree to explain the nature of the lesion. The term "rheumatic" has lost its power as a conjure word, and modern pathology demands something more satisfactory. In reading the English authorities named above it is quite evident that wherever they have mentioned otitis media as a causative agent in facial paralysis they had in mind only that comparatively small group of cases attended by a suppurative necrotic middle-ear disease. It is equally clear that, while all attributed the majority of cases to "exposure to cold," but one had any explanation to offer as to the mode of action of this agent. Since they refer explicitly to the suppurative otitis cases and do not in the other class mention the tympanic route of exposure, or, in some few instances, ridicule the possibility of the nerve being so easily affected in this part of its course, it is to be inferred that they all believe the cold produces its destruction by direct action upon the nerve-terminals or the trunk after it emerges from the stylomastoid foramen.

Upon what pathological basis can this idea rest? Undue exposure to cold may irritate a mucous membrane and readily cause its inflammation; but certainly the skin and its underlying tissues do not succumb easily to such influences. From the point at which

this nerve leaves its bony canal to its finest endings it is for the main part buried in soft tissues and protected by the skin; in fact, its protection is far better in this region than while passing through the Fallopian canal. Nor is there any analogous example of a nerve so well covered suffering paralysis from the effect of similar influences exerted upon the covering tissues.

A proper pathological study of this affection by the usual methods is not very promising. It is not at all probable that any number of cases will ever come to a scientific post-mortem investigation. In the vast majority of cases the prognosis for recovery of function is good. None are fatal; and, when death occurs to such patients from an intercurrent disease, there are many possibilities of failure to secure a valuable study of the nerve lesions. In the few cases which have been studied, the anatomical findings under the microscope were the same in all cases and consisted in a true degenerative inflammation of the nerve-fibres, with disintegration of their medullary sheaths, but no involvement of the interstitial substance—a parenchymatous and not an interstitial or general neuritis. The inflammatory destruction was always most intense in that portion of the nerve which had occupied the Fallopian canal; spread peripherally with somewhat lessening intensity; and, when traced centrally, showed in the nucleus or any portion of the nerve central from the Fallopian canal only such changes as belong to secondary degeneration from peripheral nerve injury. From the fact that the outer sheath of the nerve and its interstitial substance are supposed to have been healthy in all of these cases it has been inferred that the lesion could not have extended from diseases in the neighboring tympanic structures, and these pathological findings have been used as an argument against the possibility of such an origin for the neuritis. It is scarcely necessary to say that such an argument is not logical. It would seem perfectly possible to have an injury to this nerve result from prolonged pressure within the confined space of the Fallopian canal, where the delicate nerve-fibres would suffer while the more resistant structures of the sheath and interstitial connective tissue escaped damage. Neuropathologists recognize a "pressure palsy" as possible to any other nerve in the body; and the microscopic picture is that of a parenchymatous neuritis.

In my article referred to above I pointed out the fact that neither of the three autopsies about which so much has been written were upon cases of typical refrigeratory facial paralysis. Minkowski's⁵ case was one of a cerebral lesion. The case reported by Darkschewitch and Tichonow⁶ was a paralysis resulting from traumatism at the time of a mastoid operation, and the case of Dejerine and Theohari⁷ was probably, but not surely, one of otitic origin. Dr. L. Pierce Clark has recently reported⁸ upon the microscopic study of nerve sections taken during anastomosis operations for the relief of paralysis of the refrigeratory type. From the brief notes published it would appear that in both cases he found degeneration of the nerve-fibres resulting from compression of the nerve within the bony canal. This is a most important statement, and I regret that I cannot at present find a complete detailed report of his examinations.

I have previously referred to one exception to the general view taken of the pathology of this affection, and here I would like to quote Dr. Herter's opinion as expressed in "Nervous Diseases by American Authors."⁹ "Neuritis of the facial nerve is the cause of a very large proportion (probably more than 80 per cent.) of all cases of peripheral palsy. The neuritis is commonly called 'rheumatic.' Whatever that may mean, it is true that the palsy generally comes on after exposure to cold. Occasionally the subjects are distinctly gouty or rheumatic, but usually there is no evidence of either condition. It was formerly thought that exposure to cold caused facial paralysis by paralyzing the terminations of the nerve in the facial muscles. There is now good reason to believe that the affection always depends upon an inflammation of the trunk of the nerve (perhaps involving chiefly the sheath) within the Fallopiian canal, and there is no evidence that inflammation ever involves the nerve after it emerges from the canal."

In the absence of a definite determination of the morbid anatomy of any disease we are justified in, and must depend upon, its study

⁵ Arch. f. Psych., 1890, Bd. xxiii, p. 367.

⁶ Neurol. Centralbl., 1893, p. 329.

⁷ La Semaine Médicale, 1897, p. 453.

⁸ Jour. Nerv. and Ment. Dis., 1907, vol. xxxiv, p. 53.

⁹ Edition of 1895, p. 822.

from two points of view: first, the vulnerability of the affected tissue considered anatomically and histologically; second, the clinical features presented in a large number of cases.

Stated as briefly as possible, the anatomical course of the facial nerve after it leaves the cerebral cavity is as follows: The Fallopiian canal commences at the internal auditory meatus, above the point of entrance of the auditory nerve; it then passes externally above the vestibule into the substance of the petrous bone and, arriving at the inner tympanic wall, turns backward and proceeds along this wall above the fenestra ovalis to the junction of the posterior and inner walls, where it takes a sudden curve downwards to end at the stylomastoid foramen (Fig. 1). Until it reaches the inner tympanic wall the nerve is surrounded by the thick petrous portion of the temporal bone, and after it leaves the foramen it is well protected by the soft tissues of the neck and face. The most vulnerable point, therefore, is to be sought in that portion which rests in the Fallopiian canal with its tortuous course about the tympanum. In the bony wall of this canal there are normally, in adults, two constant openings: a small one on the *eminentia pyramidalis* for the passage of a branch of the nerve to the stapedius muscle; and the *aqueductus Fallopii*, just behind the annulus tympanicus, through which the chorda tympani enters the drum. One does not have to tax his imagination severely to conceive that infection may at times reach the nerve from the tympanum through these channels, but a little closer study will show the frequent existence of even more favorable modes of entrance than these. Politzer is authority for the statement that "that portion of the canal which traverses the tympanic cavity sometimes presents dehiscences of varying sizes," and all otologists will accept that much as true. But where and how often may these dehiscences be found?

Tomka¹⁰ says that the Fallopiian canal over the *eminentia pyramidalis* is naturally thin and frequently shows openings, and that here the covering of the nerve is in direct contact with the mucous membrane of the middle ear. He also quotes Zuckerkandl as having said that there is very commonly a fissure in the canal wall just above the oval window, probably intended for the passage of the stylomastoid artery. According to Henle the facial nerve is frequently

¹⁰ *Archiv f. Ohrlhk.*, April, 1900.

exposed in the canal, or is covered only by a fibrous membrane as in the lower animals. Embryologists tell us that the Fallopian canal in the embryo is composed of a membranous open canal, or gutter, which later becomes closed by ossification. The dehiscences come to exist as the natural consequence of any interruption to this process of bone formation. A rough examination of more than 300 temporal bones has convinced me that a perforation of some degree exists in probably one-half of the normal specimens, and that the opening is most commonly situated just above the oval window (Fig. 2).

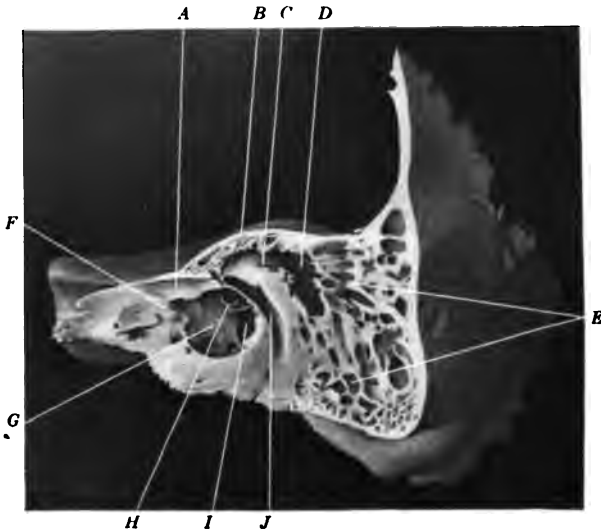
From the clinical point of view the argument is much more simple and direct. It is admitted by all that when prodromic symptoms are noticed they almost invariably include mention of the ear, if they are not restricted entirely to that organ. These symptoms are variously described as: pain in the ear, that being the most frequent one; slight deafness and stuffiness; tinnitus aurium; tenderness behind the auricle; or, earache accompanied by a slight rise of temperature and nausea or vomiting. Generally these are but transient symptoms, and the paresis makes its appearance within a few hours or, at most, two days. One will naturally ask why the ear complications have been so generally overlooked if they are so commonly present, and why facial paralysis is not of much more frequent occurrence than it is, since acute or subacute otitis media is such a common affair.

My conception of the mode of production of a facial paralysis from exposure to cold is, that something like the following occurs: the patient may be in apparently perfect health, but through exposure to cold in some way, a draught, a cold wind, or immersion in cold water, acquires an acute otitis media, which may be of a simple exudative character through the effect of vasomotor changes, or which may be the result of an active micro-organism taking advantage of the temporarily lowered resistance; in either event there is an inflammatory swelling of the mucous membrane and a pouring out of an exudate into the tympanum. If there be any break in the facial canal wall, no matter how small, sufficient to permit the entrance of fluid or of pathogenic bacteria, there exists the opportunity for a direct extension of the inflammation to the nerve or for compression of the nerve in its confined channel. We

all know that there are probably always bacteria present in the mouth and nose which can play an active rôle when the occasion is afforded, and, furthermore, that catarrhal otitis media of a mild degree is by no means rare. As a general rule these middle-ear inflammations are not troublesome, cause very little disturbance, and pass away without treatment. How frequently do we notice in association with the common cold in the head a sense of stuffiness and slight discomfort in the ear, with some deafness for a few hours or days. We pay little or no attention to the aural conditions because the pain is not great and experience has taught even the layman that the condition is ordinarily not serious. In the majority of instances where the facial nerve becomes involved, and this may occur in any case even of mild otitis if the nerve be exposed, there is only a paresis or a complete paralysis which lasts but a short time, and function is restored as the local tissues regain their normal powers of resistance and a mastery of the situation. The patient rarely mentions in these cases of paralysis the preceding ear symptoms because they have been so mild, or attracted so little attention, that when he became absorbed in the consideration of his more alarming condition, the facial deformity, he forgot the preceding disturbance.

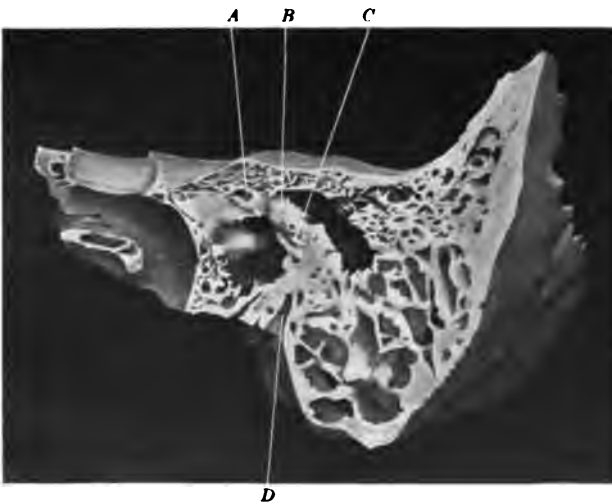
This certainly coincides with my clinical experience. Since I first spoke of this matter at the Johns Hopkins Hospital Medical Society, Dr. Henry M. Thomas, chief of the neurological department, has kindly given me the opportunity of examining many of the cases which have entered his service in the dispensary, and in every instance I have found pronounced evidences of middle-ear involvement. The constant co-existence of these affections appears to me to be more than mere coincidence. In not a single instance did the patient voluntarily inform the physician of any preceding or existing ear trouble. In most cases, the patient recalls the fact that the ear had given some discomfort shortly before the paralysis of the face appeared. In some cases the aural discomfort still persisted, but its existence was ignored by the patient because of his deeper concern in the facial deformity. But, regardless of the subjective sensations, there was positive objective evidence of ear disease in all of the cases, though there were many variations in the tympanic picture. In but one case have I observed an acute inflam-

FIG. 1.



Section to show tympanic wall, stapes *in situ*, and facial nerve canal. Just above stapes is common site of dehiscence. *A*, canal of tensor tympani; *B*, tegmen tympani; *C*, aditus; *D*, antrum; *E*, mastoid cells; *F*, inner wall of tympanopharyngeal tube; *G*, promontory; *H*, stapes and stapedius muscle; *I*, round window; *J*, canal of facial nerve.

FIG. 2.



A specimen of temporal, showing natural dehiscences in facial canal. *A*, large dehiscence above oval window; *B*, bony wall of facial, so thin as to be translucent; *C*, series of small openings into facial canal; *D*, lower end of facial canal.

FIG. 3.



View of membrana tympani showing hyperemia, the vessels extending out from the periphery, a condition of mild, acute or subacute otitis media; a contrast to the intense and complete redness of membrane with more severe forms of middle-ear inflammation.

FIG. 4.



Membrana tympani as it may appear when there is a fluid exudate in the tympanum; line of demarcation shows height fluid has reached. No other visible evidence of inflammation.

FIG. 5.



Site and form of incision to evacuate tympanic cavity of inflammatory exudate.

matory condition of the membrane, and that patient was seen on the day following the onset of the palsy. In all the others there existed the picture of a subacute (Fig. 3) or chronic catarrhal process. In some of the cases a line of demarcation on the drum-head showed the evidence of fluid in the tympanum (Fig. 4) and a paracentesis proved the correctness of the diagnosis; once only was this secretion purulent. One of the most interesting cases I have seen presented such a remarkable middle-ear condition that I would like to speak of it more fully.

The patient was a woman aged 34 years, who came in with a left facial paralysis of seven months' duration. When asked if she had ever had any ear trouble she stated that she had suffered some pain in her left ear just a few days prior to the paralytic attack and that she had been deaf on that side ever since. The paralysis had come on suddenly, was supposed to be due to exposure to cold, and the usual line of treatment had failed to produce any improvement. Inspection of the ear showed a dull, apparently thickened membrane with no light reflex. There was a very marked loss of hearing for low tones and the Weber test was lateralized to the affected side. Although the period of delay had been very long, I advised a tympanotomy. The operation was performed by my associate, Dr. E. H. Schild, who reported to me later that when the knife punctured the membrane he felt as if he was cutting into a doughy substance. I immediately examined the case with him, and, through an enlarged opening, we could clearly determine that the tympanum was partially filled with a firm clot of blood which was certainly not of recent origin. By frequent irrigation, Politzerization, and the use of absorbents, the clot was broken up and removed and within a few days there was marked improvement in the facial condition. The patient recovered the full hearing power and the paralysis entirely disappeared. This was the second instance in which I had encountered a semisolid exudate in the tympanic cavity.

I reported some of these experiences and conclusions to the American Otological Society in 1904, and my experience up to that time had led me to believe that an inspection of the tympanic membrane would show in every case of the so-called refrigeratory facial paralysis the existence of a middle-ear inflammation or the

products of a recent inflammatory process. I had so expressed myself before a local medical society; and when told later that some cases had been submitted to an aural examination and that the aurist had reported finding nothing abnormal about the ear, I felt that either the examination had been imperfect or that the examiner was looking for some gross lesion and failed to note the changes which, though slight, were of great importance. About this time, however, I received a letter from Dr. Norton L. Wilson, of Elizabeth, N. J., which caused me some concern. Dr. Wilson's ability to examine the tympanic membrane could not be questioned, and his interest in the subject was sufficiently vouched for by a paper on facial paralysis which he had published in *American Medicine* (Feb. 13, 1904, vol. vii, p. 266). The problem he suggested to me was embraced in the following paragraph: "I have the histories of nine or ten cases in which I could find absolutely nothing in the middle-ear picture. I recognize that what you say is logical and should be so, but I have not seen the proof that it is so." For a considerable time this perplexed me sorely. I could not answer Dr. Wilson because there was no reason for doubting either his powers of observation or the honesty of his examination and report. Yet I was still seeing an occasional case and always finding tympanic changes. In the course of time the opportunity came to learn the answer, and to-day I believe I have evidence that we were both right, as the following case history will show.

In the spring of 1906 Dr. William T. Watson, a fellow practitioner of this city, and a very careful clinical observer, telephoned me that he had under his care a case of refrigeratory facial paralysis that refuted my theory of a coexisting otitis media; he had made an otoscopic examination and was satisfied that both membranæ tympani presented a normal appearance. The paralysis had existed three days, but he would like me to examine the ears; and I gladly accepted the invitation. Upon examining the tympanic membrane I was forced to admit that it would not be possible to convince any sceptic that this membrane was abnormal; I felt personally sure of a slight difference between the two membranes, but this difference lay only in the appearance of that moderate peripheral hyperæmia that is suggestive of a receding tympanic inflammation; and I could not fairly expect even an otologist, if he doubted the theory,

to consider it as sufficient evidence of a diseased tympanic cavity. Unwilling to accept defeat, and searching for some other proof of middle-ear disease, it suddenly occurred to me that in the hearing tests we have an excellent means of diagnosing middle-ear disease.

So far as was known this young man had been perfectly normal in every respect; a healthy, well-developed lad of the working class. He was engaged in a tailoring establishment, and towards the close of a hard day's work, having become overheated, he stepped out of doors and sat for some time in his shirt sleeves in the cold air. When he arrived home that evening he complained of feeling badly, had symptoms of a cold in the head, and retired early on that account. He spent an uncomfortable night, and appeared the following morning with a complete paralysis of the right side of his face. So much of the history was furnished by the patient. Further than that his whole attention was centred in his deformity and a consideration of whether it was likely to be permanent.

While questioning him regarding his sensations of the night before the paralysis appeared, his sister volunteered the information that he had complained a good deal of earache, and this statement was later endorsed by his mother; the patient had forgotten it, but recalled the fact when reminded of some conversation at home. I state this in detail because it is such a clear example and explanation of the absence of reference in clinical reports to that transient earache which probably exists in the majority of cases. The horrible deformity so thoroughly fills the mind of patient and relatives alike as often to obscure completely the conditions existing immediately before its appearance.

Of the objective examination of the ear I have already spoken; call it an apparently normal tympanic membrane. The hearing tests with tuning forks gave the following result:

	Right.	Left.
Lower tone limit	C(128)	C(26)
Upper limit, Galton	0.5	0.5
Bone conduction C(512)	10/10	10/10
Air conduction C(512)	12/20	20/20
Weber, lateralized to the right.		

The left ear was entirely normal. In the right there was normal bone conduction and perfect perception of high notes, accompanied by a loss for low notes and diminished air conduction, with the

Weber test heard best on the affected side. In other words, there was some lesion of the transmitting apparatus on the right side. With a clear external auditory canal and a normal tympanic membrane this could only be an exudate in the tympanic cavity. Under proper aseptic precautions, a tympanotomy was performed and several drops of a clear serous fluid exuded. In 24 hours there was a marked change in his facial expression and in 72 hours he had entirely recovered from the paralysis without any other treatment.

From this case I think we may learn several very valuable points. In the first place, it is quite possible to have a considerable exudate in the tympanic cavity without external evidence thereof on the drumhead. Secondly, an apparently normal drumhead does not necessarily mean that there is not or has not recently been a marked intratympanic affection. Thirdly, our examination for middle-ear disease is not, in doubtful cases, complete with a simple inspection of the tympanic membrane, but if evidence is not discovered there we must resort to other means of examination. Fourthly, in the hearing tests, especially those made with the tuning forks, we have a delicate but satisfactory means of determining the existence of middle-ear disease.

One other case of similar character has since come under my observation. On April 30, 1907, Dr. H. M. Thomas referred to me Miss N. S., 39 years of age, with the following history: Complete right-sided facial paralysis of one week's duration. Good general health. Had an attack of tonsillitis in February, and was under a great deal of nervous strain for some time afterwards. For ten days prior to the appearance of the paralysis she had a severe cold in the head with constant unpleasantness in the right ear; there was no distinct pain, but a feeling of stuffiness. Paralysis occurred on April 23, after a day or more of suffering with "neuralgia." When examined, one week later, the left tympanic membrane appeared normal and the right showed only a slight hyperæmia about the periphery, with a shrinking of the light-cone—the apex of the cone alone remaining. Hearing tests disclosed a normally functioning left ear and these interesting points in the right: air-conduction reduced to $20/30$; Weber referred to the right; and not only a loss for the deep bass notes, but any low note caused painful sensations—clear evidence of middle-ear disease in an ear

presumably normal prior to the present illness. She had been under observation a week without any apparent change in the facial condition. An anæsthetic was administered at the hospital and a free incision made in the right tympanic membrane. With the aid of a Eustachian catheter, a fluid exudate was forced out of the tympanum and a cover-slip examination showed the presence therein of a few pneumococci. The operation was performed in the early afternoon. That same night she noticed some improvement in the movement of the eyelid, and two days later she could close the palpebral slit to within 5 mm.; on the following day the lids closed to within 3 mm., and on the sixth day completely. On May 20 she had entirely recovered from the paralysis and hearing had returned to normal.

Now the question has been raised whether, after all, the coexistence of a mild otitis and the facial paralysis may not have been a mere coincidence. I would like, in this connection, to put on record two cases that I have had the privilege of studying carefully both before and after the appearance of a refrigeratory paralysis of the face. They seem to me to prove most conclusively, from the clinical point of view, a causative relationship between the two affections.

Mr. E. T., aged 44 years, was seen at the Peninsular General Hospital, Salisbury, Md., June 3, 1905, complaining of commencing deafness. For six months he had noticed some difficulty in hearing ordinary conversation; and as his official position required close attention to Court work, any delinquency of hearing was likely to prove embarrassing. He was found to be suffering from a mild subacute otitis media and chronic nasopharyngitis, with hypertrophied turbinates and a spur on the nasal septum. An appointment was made to operate upon the nose at my July visit to the hospital. He failed to keep the appointment, and when in September I inquired about him, I ascertained that within a few days after I had seen him he developed an acute exacerbation of the rhinitis, with pain in one ear, and, after one day of this, a facial paralysis. When I next examined him there was a marked change in the tympanic picture on the affected side, decided evidence of an increase in the inflammatory affection there over the old condition. I was not permitted to treat him, but I learn that the paralysis slowly improved and after many months' delay his face became fairly straight.

The second case is much more striking and interesting. A dispensary patient in the Baltimore Eye, Ear, and Throat Hospital, a large, healthy colored man, was admitted to the ear department because of an acute exudative (catarrhal) otitis media. By the use of hot applications, catheterization of the Eustachian tube, and systemic treatment, the middle-ear inflammation subsided. He visited the clinic a number of times and was almost well; in fact, we were only trying to make sure that his hearing power had returned fully to normal. Suddenly he came in one day in great distress, saying that he had "caught a fresh cold" two days previously and had that morning awakened with a facial paralysis on the left side. The tympanic membrane was congested, most intensely in the upper portion, but throughout there was a sense of dulness or stuffiness and deafness quite marked; earache had occurred the night before but was not severe. The paralysis was unilateral and complete; the opposite side of the face and the right ear were as when seen at the last visit. An incision was made into the tympanic membrane at once, a serous fluid exuded, and, 72 hours later he was exhibited at the Johns Hopkins Hospital Medical Society with a healed membrane and complete recovery from the paralysis.

The histories of these two cases are precisely like those of nearly all published cases of refrigeratory facial paralysis, save for the knowledge possessed by previous examinations of the ear. In my opinion, they are typical of what transpires generally in that affection.

The practical aspect of the whole matter is this: If refrigeratory facial paralysis is brought about indirectly through the action of the cold upon the nasopharynx and middle ear—an acute or subacute otitis media being always produced and the intratympanic exudate in turn acting upon the exposed facial nerve, whether through exerting pressure upon its delicate fibre structure or exciting inflammation of the sheath—we have not only a simple and satisfactory explanation of a hitherto obscure problem in pathology, but have reached a most important stage in the treatment of the affection. In the majority of cases the tendency is toward recovery of function in the course of time, with or without treatment. Recovery is usually slow, however, and may require many months.

Here we have the means of securing quick results if only the case be taken up promptly. The tympanum must be opened and the exudate removed. This is easily accomplished while the inflammatory products are fluid, but very difficult when they have become organized; here the pressure will to some extent be continued until absorption can be brought about. An early paracentesis, then, is the treatment; and results are likely to be satisfactory just in proportion to the promptness with which treatment is instituted. The earlier the tympanum is opened the easier it will be to evacuate its contents and the more rapid will be recovery of muscle function. In every case of refrigeratory facial paralysis the ear should be carefully examined immediately, and if there be the slightest reason for supposing the existence of middle-ear trouble the tympanum should be opened (Fig. 5). In fact, I am personally prepared to urge tympanotomy in every case at the earliest possible moment, even when you cannot see evidence of intratympanic inflammation, because, as I have pointed out, there probably is disease there which is not visible to the eye; usually the hearing tests will prove this, and these tests are simple enough for any practitioner to master. However, you err on the safe side, if at all, in doing a paracentesis. A clean incision through the tympanic membrane can do no harm; if there be no disease there, the wound will promptly heal, without any damage to function. The best that any other form of treatment offers is weeks or months of general treatment of a haphazard sort and a prayer for a satisfactory eventual outcome.

I hear you say: this is an enthusiast who happens to have seen a number of cases in which there was coincident ear disease, and, if we admit that the theory is true of some cases, the general application to all refrigeratory cases is entirely too broad and unjustifiable. My answer is, examine your cases and you will find the same conditions. But it happens also that I can give a better answer and one that if not more true will at least receive more consideration. The fact does not rest upon my say-so, nor upon that of any other otologist. One for whom you have the most profound respect, perhaps the greatest of neurologists, has said the same thing, except that he applied it to *many* instead of *all* cases, and therein I think he was too conservative. Let me call your attention to, and fur-

nish a brief abstract from, a "Lecture on Facial Paralysis" by Gowers,¹¹ delivered in 1893.

"Complete paralysis of the right side of the face, in a child of seven, who presents no other symptoms—that is the problem before us. You have heard the questions asked, and the answers given by the child's mother, and that we found no evidence of a cause. You heard the mother give a negative answer to every inquiry—there had been no blow, no exposure to cold, no discharge from the ear. Those are the three chief causal facts to be considered in every case. But one other question was asked that should never be omitted in such cases: Has the child suffered from earache? *The mother then remembered a fact that had been forgotten, remembered it with surprise, so little had she connected it with the affection of the face.* . . . When many of those who now teach first studied medicine, they were taught that the nerve-endings were the seat of the lesion in the commonest forms of facial paralysis—that which follows exposure of the side of the head to cold. The cold, acting on the surface, was assumed to act on the nerve-endings in the muscles of the face. This pathology was purely hypothetical; no evidence of it had been ascertained, and there was no demonstrable analogy that could be produced to support it. Indeed, it now seems to us strange that the opinion should have been accepted so generally, since a little consideration will show how great a difficulty there must have been in adjusting it to the facts. Why should cold act upon the extremities of one nerve, upon all of that up to the middle line, and no further, not a single muscle or fibre on the other side? Why should the effect of cold acting on the surface be absolutely limited to the endings of one nerve? This difficulty does not seem to have been recognized. When increasing precision of observation, and a wider comparison of facts, suggested irresistibly that such a paralysis must be due to a process acting on the fibres where all are near together, and when it was discovered that this was the true pathology of infantile palsy, the idea that disease of the nerve-endings was the cause of paralysis disappeared. . . . If there is no history of discharge, disease of the ear is not likely to be the cause. But this rule, true of facial paralysis in general, is not invariably true of it. Exceptions are met with, and this case is an

¹¹ Clinical Journal, London, 1893-4, iii, 241 to 248.

illustration of that fact. . . . Exceptions to the rule that obtrusive signs of caries long precede facial paralysis which results from otitis, depend upon the anatomical conditions of the ear. That has not indeed been proved, but we know that exceptional conditions often exist; they explain that which would otherwise be inexplicable, and which nothing else explains. In some cases, the facial nerve is separated from the tympanic cavity by a layer of bone so thin that inflammation can readily pass from the cavity to the nerve-sheath. In such, bone disease is not necessary for the extension of inflammation to the nerve. It is not enough to ask if there has been a discharge. Discharge generally means disease of the bone; disease of the bone is the common cause of secondary facial paralysis, but the nerve is sometimes affected by extension when there is no bone disease."

If in connection with that lecture of Gowers' you will read the Thesis "*De l'Étiologie Otique de Certains Cas de Paralysie Faciale Dite à Frigore*," presented to the Faculty of Medicine of Lyons by Camille Bouthoux in 1870, and published in 1894-5, vol. lxxxv, a masterpiece in the review of the whole subject from every aspect, you must be convinced of the following conclusions:

1. In refrigeratory, or so-called rheumatic, facial paralysis there is always an intermediary subacute otitis media between the time of exposure to cold and the appearance of the palsy.

2. In every case of this disease it is your duty to make or have made a careful examination of the ears, not alone for suppurative affections of that organ, but, more particularly, for mild exudative middle-ear disease.

3. If inspection of the tympanic membrane does not disclose satisfactory evidence of middle-ear disease, employ the hearing tests, especially the use of tuning forks, before deciding that there is no middle-ear lesion present.

4. There is abundant proof, both clinical and anatomical, of the relationship between the ear affection, as a stage of the disease, and the paralysis; which not only makes clear the pathology, but provides an easy and promising form of treatment.

5. Prompt aural treatment will cure the paralysis, and the rapidity of cure depends upon how early middle-ear treatment is instituted.

Proctology

ANORECTAL FISTULA AND ITS TREATMENT *

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THE description of the following case serves well to illustrate certain questions concerning the development and operative treatment of anorectal fistula.

The patient is a girl aged fourteen years who is suffering from anorectal fistula, or, to be more exact, anorectal fistulæ, as there appear to be two fistulous tracts which are entirely separate and distinct from each other. However, we cannot be absolutely sure concerning this feature until the sinuses have been opened. It is often found at the time of the operation that these tracts communicate with each other, whereas in the beginning they seemed to be separate and distinct. From the history of this case, however, I take it that we have two distinct fistulæ to deal with.

This girl, who, as I have said, is but fourteen years of age, lives in the interior of Kentucky; she weighs 95 pounds, height 5 feet 5 inches. She is a fairly well developed girl for one of her age. She has been in excellent health all her life, according to the history we have obtained, having had no diseases even excepting measles. While she has continued to gain height, her weight hardly equals now what she weighed at the age of twelve years, at a time preceding the beginning of the fistula, for it has been kept down by the continuous suppuration and the effects thereof on her general system. The trouble from which she is now suffering began two years ago.

The girl was attending school at that time and walked about three miles each day; she was a healthy, robust young girl. Two

* Clinical lecture delivered at the University of Louisville, Medical Department.

abscesses appeared simultaneously, one in either buttock; the one on the right side was opened, the other left to rupture of itself. Emphasis must be laid upon the fact that these abscesses began at the same time, for this is perhaps the chief reason why it is possible to assume that we have two distinct fistulæ to deal with. Ordinarily where openings are found in both buttocks resulting from fistulæ, we believe there is some communication between them; that is the rule excepting in those cases where the abscesses appear at the same time. Even where such abscesses appear simultaneously, we sometimes find there is a communication, and the condition is simply one of complex fistula, *i.e.*, we have one sinus with a number of branches. Where the abscesses appear together, the chances are that there are two distinct and separate fistulæ. The reason for this is that where one abscess begins and results in fistulous extension the pus is likely to burrow around into the other buttock, more likely in fact than that there should develop subsequently a separate and distinct abscess in the opposite buttock.

In this case there is no history of injury so far as we can ascertain at present. However, the patient thinks she may have injured herself by falling while at play with other children. She is not positive about this; in fact, only when the direct question was put to her was she willing to admit such a possibility. There are several reasons why it is important to know, in this particular instance, if these abscesses occurred as the result of a bruise, a fall, a kick, or injury of any kind.

Remembering that this girl has grown very rapidly, that she is large for one of her age, that there is no history of injury or any other trouble whatsoever, we are at once reminded that in more than 50 per cent. of the cases of anorectal fistula the tubercle bacillus is largely responsible for the mischief and that in about 18 per cent. of all cases it has been found that the tubercle bacillus alone is responsible. I mention this point especially to bring out what I deem a fallacy, *viz.*: I understand that some observers consider all anorectal abscesses as tuberculous in origin. That is going to an extreme, and it is easily proven not to be the case. We have such abscesses and fistulæ resulting from other forms of germ action—the streptococcus, staphylococcus, and colon bacillus.

From the family history it is learned that her mother and

father are both living. Her mother, so far as I can learn, is a healthy woman; her father is a robust man. She is the only child. Her grandparents are living and are healthy old people. There is no history of consumption that can be found in the family, nor in the uncles or aunts on either side.

These abscesses were the first sign of any serious trouble. She says they made her very sick, that she developed high fever, and she was in bed for about three months. In the meantime she lost considerable flesh, but finally recovered sufficiently from the illness to get up and about. These sinuses, however, continued to discharge more or less all the time. One or the other would apparently heal and the discharge would cease for a time, *i.e.*, the external opening would heal and remain closed for a week or two, then reopen and the discharge would again be noted. Then the sinus on the opposite side might heal and the discharge cease, only to reopen in a short time. I believe at one time both sinuses closed simultaneously, and remained so for a week, leading the parents to believe that there had been a spontaneous cure. Of course the patient has suffered considerable pain from the presence of the pus within these sinuses.

In a few words I believe the best and most expressive definition of a fistula is that it is nothing more nor less than a contracted but unobliterated abscess cavity. A circumscribed suppurative process is, of course, an abscess. The abscess gradually enlarges, it presses in all directions, and finally becomes very tense; then the pus makes for itself additional room in one or more directions, and eventually opens externally. This opening, however, may be upon either a mucous, serous, or cutaneous surface. If the abscess ruptures into the bowel, it has opened on a mucous surface; if into the abdominal cavity, it is upon a serous surface; if upon the buttock, it is a cutaneous surface. When an opening occurs, either by the abscess rupturing of its own accord or if it is opened by the surgeon's knife, pressure from within at once ceases, the pus rushes out, and the walls of the abscess collapse; the pus drains out, and finally the abscess walls contract closer and closer until in the end we have a contracted but an unobliterated abscess cavity, *i.e.*, a fistula.

It is well to remember that the action of the pus-producing

organisms upon healthy tissue is such that we have offshoots from the abscess in various directions, and an offshoot may extend out into the tissues for a greater or less distance, according to the resistance offered, the character of the tissues, etc.; and, finally, after opening of the abscess has occurred, either spontaneously or by the surgeon's knife, we will have these offshoots remaining as branches of the main sinus. Thus it is clear that we rarely have a simple fistula, a fistula with a single sinus without branches or ramifications in various directions. The rule is to have a number of branches. The extent of the fistula depends very much upon the form of the abscess which preceded it.

For the sake of convenience, for clinical purposes, we may divide anorectal abscesses in general into four chief varieties: the subcutaneous, the ischiorectal, the submucous, and the perirectal. In addition to these, in the male may be found abscesses having their origin in the prostate gland or deep urethra. Of all fistulæ the simplest and easiest to cure is, of course, the one resulting from a subcutaneous abscess, for in this the fistulous tract is superficial to the deep fascia and muscular tissue and can be easily eradicated, the use of local anæsthesia only being necessary to perform the operation. The fistula caused by the ischiorectal abscess is much more serious. In such an abscess the pus, being confined in the ischiorectal fossa, burrows in every direction, finally making for itself an exit at the point of least resistance, which is frequently into the bowel between the two sphincter muscles; or it may make its way through the incomplete stratum of fascia between the fat of the fossa and the subcutaneous tissue, finally emerging from one or more openings upon the surface of the buttock. Again it may pass entirely around the bowel and invade the opposite side. A submucous abscess originates in the submucous tissue of the lower two or three inches of the rectum. Fistulæ developing from this form of abscess are comparatively infrequent, yet deserve special attention because so easily overlooked. Submucous fistulæ are among the most potent causes of pruritus of the anal region. In the perirectal abscess, originating in the loose connective tissue above the levator muscle and between it and the rectum, the pus makes its way into the bowel high up, or possibly invades the ischiorectal fossa. In operating for fistula caused by this variety

of abscess, the wound is necessarily a deep one and great care must be exercised in the postoperative treatment to see that the sides of the wound do not adhere and that granulation tissue may form solidly from the bottom.

If an anorectal abscess is seen early enough, and is given the proper treatment, a fistula can nearly always be prevented. Free evacuation of the abscess should be brought about just as soon as pus is known to be present. It is better to open too early than not early enough. The manner of opening the abscess is of the greatest importance. It is a mistake to depend upon a simple puncture, or even a linear incision, into the abscess. The object is not only to let out the pus but to provide free drainage until the cavity has entirely healed. The best way to accomplish this is to make use of the T-shaped or crucial incision, extending each extremity of the cut not only through but slightly beyond the inflamed zone. All septa should then be broken down and the interior of the cavity cleansed to the healthy tissue. The projecting corners should be trimmed off, thus rendering it impossible for the edges to adhere and for the surface of the wound to close before the base has healed.

I desire now to say a word or two in regard to the operation for fistula. The text-books on general surgery, especially the older ones, advise that anorectal fistula be operated upon about as follows: Insert a grooved director into the sinus, lay open the tissues freely, and pack the wound with gauze! That is about the extent of the treatment given. *Fistulæ* treated in this way will not get well—not one in a thousand! Instead of saying, “incise the tissues,” or cutting through the tissues down to the sinus, the word *excise* should be used; excise the fistulous tract or tracts with the various branches that may be found, cut away all diseased tissue, and pack with gauze; then the wound will heal and the patient get well.

Another point in regard to the operation: Many times doctors think we cut recklessly in operating for fistula. There are times when it is necessary to cut in a way that appears to be reckless, but it is necessary to know just what you are cutting; there are certain structures that we cannot cut away freely, and there are certain others which we can. If a sinus exists well out on the buttock, we can cut away the greater part of this without doing

any especial damage, but when we are cutting around the sphincter muscle, of course, it is necessary to exercise the greatest care. One may cut through the external sphincter muscle once at a sitting without any fear whatever, provided the sphincter is not detached from the neighboring structures. If, however, as a result of long continued suppuration the sphincter muscle has been detached from the surrounding attachments, as sometimes happens, perhaps for one-third or even one-half or more of its circumference, then division of the muscle will permit the ends to retract so far, since there are then no surrounding attachments to support and hold it in place, that the severed ends will not reunite and as a consequence there will be permanent impairment if not total loss of the function of the sphincter. If the sphincter muscle is severed it should be cut squarely across the muscular fibres. It is a mistake ever to cut obliquely across the sphincter muscle.

There are several openings about the anus in the present case. That is not unusual. The most unusual feature of this case is the presence of the disease itself in so extensive a form in one of this age. While it is true that fistula is found at all ages, even occasionally in the infant a few weeks old, yet, comparatively speaking, anorectal fistula in a girl of this age is extremely rare. It is but seldom that we observe anorectal fistula in persons under twenty years of age, and especially is this true in the female.

The patient being profoundly under the influence of the anæsthetic, as is necessary always in operating upon the rectum, the first step is to examine the external openings, and the sinuses as they traverse the tissues. With a grooved director, or preferably with a small blunt-pointed probe, the sinuses may be carefully explored. At several points it appears that a sinus has partially healed, but slight pressure with the probe proves that a continuation of the sinus exists beneath. As is usual in such cases there are many branches communicating undoubtedly with the main sinus in the deeper tissues about the buttock. The probe can be inserted with ease in various directions. A grooved director may be introduced into each of the sinuses and the overlying tissues carefully dissected off. The director can be inserted easily in several of the sinuses which are quite large. Inserting a finger into the rectum one should try to determine whether or not any of these openings

extend into the bowel. By exerting slight pressure on the probe, and by pressing outward with the finger in the rectum, one can easily demonstrate whether or not any of the sinuses extend through into the bowel. It seems that the destruction of tissue has been more or less lateral. There is no opening into the bowel on the right side, but one may exist on the left side, or, as is often the case, in the posterior median line. This will be determined later. In handling the probe or grooved director caution should always be observed to press lightly, otherwise a false sinus may be made, as it is quite easy to make an opening where none exists in the loose tissue.

The main sinus on the right side being laid open, the numerous small branches can be easily seen. It is necessary to follow and carefully divide all these. This may be done with scissors or a bistoury, the former in my opinion being preferable. Referring to my remark a moment ago in regard to the cutting necessary in these cases: Far out on the buttock of course one may cut freely, and if a blood-vessel is severed hemorrhage can be easily controlled. With a pair of prong forceps the flaps of skin are pulled up and carefully cut away, thus endeavoring to convert our wound as nearly as possible into a "surface wound." At one point we find quite a large piece of apparently healthy tissue, but immediately underneath it there exists a suppurating sinus, and in order to make the operation complete and secure healing from the bottom it will be necessary to sacrifice all the overlying tissue. It is absolutely necessary that this be removed to secure the best results. All cicatricial tissue surrounding these various fistulous tracts must also be cut away, and all the fistulous tracts as well as the tissues overlying them excised. After dividing some of the smaller sinuses they are curetted thoroughly in order to make sure that all the diseased tissue is removed, for if any part of the sinus was left pus would continue to be formed, and the purpose of the operation defeated.

Proceeding to the left side the same methods are repeated. After laying open the main sinus the underlying tissues appear very dark; there are branches running in all directions which must be followed up carefully and dissected out. If there is a communication between the two main sinuses on the two sides, the condition

would be essentially a horseshoe fistula, and it would probably take the patient a long time to recover, especially if there is destruction of tissue as far as the bowel. The work, as you will observe, has to be done piecemeal, so to speak, in order that we may not unnecessarily sacrifice healthy tissue in assuring ourselves that all diseased structures have been eliminated, for we will save all the healthy tissues that we consistently can. The most tedious part of the procedure is the search for the various branches of the fistula. Much information can be gained by the finger, as the sensation imparted to the examining finger by the hardened tissue is quite characteristic, and by this means we can oftentimes detect a fistulous tract which might otherwise be overlooked. On the left side there is a large mass of adipose tissue above one of the main sinuses which would interfere with the healing process, therefore it will be cut away.

The complete excision of all diseased tissue on the left side, as was done on the right, leaves a very large open wound on both sides. This extensive cutting is necessary to remove all the fistulous tracts. While the wounds are apparently quite deep, they will rapidly fill in with healthy granulation tissue, and there will be little or no deformity after the healing process is complete, and there will not be any extensive scarring. An operation such as this, if done carefully and with the same precautions as to asepsis that are observed in operating elsewhere, should result in no greater deformity or scar than after operations in other localities where healing is expected by granulation. While in this case there existed some pus to start with, still aseptic precautions, for obvious reasons, are just as necessary, or even more necessary, than if there had been no suppuration.

The wounds are carefully packed with plain sterile gauze "ruffled" in order to prevent postoperative hemorrhage. While immediately after the operation there is no bleeding, except for some slight capillary oozing, yet after the patient recovers from the effects of the anæsthetic there might be some hemorrhage, and this we desire to prevent. For that reason we pack the wounds tightly with gauze. Iodoform gauze, which was formerly used for this purpose, is absolutely unnecessary. The gauze packing is permitted to remain intact for forty-eight hours; by that time

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it can be more readily removed than if an attempt were made to take it out at the end of twenty-four hours. Over the gauze a large piece of cotton is placed which will be removed at the end of twenty-four hours. When the gauze is removed after forty-eight hours the wounds are irrigated with saline solution or plain sterile water, and again packed in the same manner except more loosely. Following this the wounds are irrigated and dressed every day.

In packing with gauze the wounds left after operation for ano-rectal fistula, care must be exercised to see that the gauze extends to the bottom of the wounds, that the tissues are kept separated, in order that granulation may begin at the bottom. If the edges are allowed to adhere, a cavity might persist at the bottom of the wound, pus would soon collect, an abscess would be the result, and consequent recurrence of the fistula would be inevitable. If the diseased tissues are carefully trimmed away, and the wounds packed in the manner indicated, prompt healing by granulation may be reasonably expected.

After application of the cotton a "T" bandage is used to keep the dressing in place. In some cases hemorrhage at time of the operation is not so readily and so completely controlled, and in such instances greater pressure over the dressing is desirable. To secure this a "perineal bandage" can be employed, using an ordinary wide roller bandage of firm material—not gauze. By tying this tightly around the waist and then passing it forward and backward over the dressing any desired degree of pressure can be exerted. If there is slight bleeding after the dressing is applied, pressure from the binder will be sufficient to control it.

In about a week after the operation these wounds will have lost their raw flesh-like appearance, they will have become quite red, and be covered with soft velvety granulations. After the wounds are well covered with this granulation tissue the danger of infection is much reduced, but great care should be observed in handling wounds of this character until they are covered with granulation tissue. I do not mean to say that after this has taken place care should be abandoned, as a matter of fact it should not, but especial care should be exercised before. I am aware it is a common idea that rectal operations do not require the care as to asepsis generally observed in surgery elsewhere.

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That is a great mistake. The wounds after operations on the anorectal structures should be dressed with the same aseptic precautions as would be observed in the management of surgical wounds elsewhere. But, as I have said, after these wounds are covered with granulation tissue they have then greater power of resisting or throwing off infectious material that may possibly come in contact with them than before granulations appear.

Sometimes it will happen that these wounds are somewhat sluggish in healing, and especially is this true in patients of low vitality. And, indeed, a good many cases of fistula are found in persons of rather low general vitality. The reason for this is quite plain. Persons who are unhealthy, reduced in vitality and normal resistance, are more likely to develop abscesses than those who are perfectly well and strong. Then, again, if an abscess develops as the result of injury, the person at the time being otherwise perfectly well, the mere fact of the existence of the fistula for months or perhaps years results in a greatly lowered general vitality.

In cases where the wounds do not heal as rapidly as they should, if they are not well covered with healthy granulation tissue at the end of a week, what can be done to stimulate the healing process? There are a number of methods which may be applied. I will mention but one, viz.: the use of compound tincture of benzoin, liberally painted over the entire raw surface or surfaces. This may be repeated in two to four days, depending largely upon the effect of the first application. In tubercular subjects especially do we find applications of benzoin or some other similar preparation necessary. It is a well-known fact that wounds of this character in tubercular patients heal rather slowly and stimulating applications are necessary.

If the wounds rapidly become filled with granulation tissue from the bottom, as occurs in favorable instances, at the end of the second week one may observe a white line at the junction of the raw surface and the skin. This white line, of course, means new skin which is gradually encroaching upon the wound. Another process which assists the healing of what may look like a very large wound, is contraction that takes place in all wounds of this character. Even without allowing for the newly-formed skin which

gradually encroaches upon the wound surface on all sides, the wound itself will contract so that the open surface, which may at first be five inches or more in length, at the end of a week or two will not be more than four and a half inches. In the healing process the skin does not run over the wound, so to speak, but continues to extend toward the centre from the edges, the formation of new skin being governed entirely by the healing of the cavity itself. The new skin never dips down into the cavity of a wound, it forms only around the edges, which is a wonderful provision of nature.

As these wounds are very extensive and deep, of course you will naturally ask how much depression there will be left after the healing process is complete. I can promise you that there will be very little if any depression. The skin does not creep over from the edges of the wound until the part has become rounded out almost to a normal outline; in other words, the deep cavity is first filled with healthy granulation tissue, then the skin gradually extends over it. One is often surprised when the healing process is complete to see the scar; instead of there being a large flat depressed surface, there will simply be a linear scar to mark the site of the operation. Of course the skin over this surface will show some discoloration; for possibly two or three months it will be whiter than normal, but the scar itself will be linear; gradually the parts will become softer and after the wounds have entirely healed, say in six or ten weeks according to the vitality of the individual, there will be little or no deformity.

Psychiatry

ILLUSTRATIONS OF THE ADVANTAGE OF PSYCHOMETRIC METHODS IN DIAGNOSIS, PROGNOSIS, AND TREATMENT OF CEREBRAL DISORDERS

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WHILE it is true that in the last resort the estimation of the insanity of an individual must be a question of and depend upon his conduct, yet such appreciation of his psychic reaction as is afforded by experimental mensuration must needs be invaluable in enabling the examiner to determine a mental enfeeblement which inevitably connotes insane conduct under suitable circumstances.

This thesis, I am aware, has often been disputed; for many psychiatrists believe that the exactness of psychometry can never replace the diagnostic acumen derived from experience, the "*Je ne sais quoi*" of the old asylum physician.

On *a priori* grounds it would be very strange that that branch of medicine which concerns itself with the disordered functions of the cerebrum should persistently remain in the rear of the advances in methods now occurring in the various other branches of clinical medicine, and that psychiatry alone should be refused the precision obtainable only by the quantitative method¹ which has contributed so largely to the clearer knowledge of disease obtained by the study of clinical medicine as a whole.

But the constant appeal of the conservative is to the practical; and it is to that appeal that I wish to respond by reporting the following examples in which the quantitative method has proved of inestimable service, first in the diagnosis and later in the prognosis and treatment of the cases.

CASE I.—Physician, aged 36, referred by Dr. A. B. Howard of Cleveland, Ohio, and examined December, 1907. For a year or

more he has felt heavy and bilious; he thought this was due to auto-intoxication, for he had been a heavy eater and a great drinker of coffee, although he did not smoke and took alcohol only rarely, and then never more than one bottle of beer in a day.

The previous and family histories are insignificant, except that some seven years ago he poisoned his finger during an obstetrical operation. The ulcer which formed, he believed to be a streptococcus infection, and he treated it as such during the two or three months it existed. He declares that he did not suspect it of being syphilitic, and that he saw no secondary symptoms.

He married at 24 and at 32 lost his first wife, by whom he had three children ranging from 12 to 7 years old and all healthy. After four years he married again, and has by his second wife a healthy child one month old.

Present Illness.—Last May he felt a dull heavy pain in the left sacral region, especially after prolonged sitting in his buggy while on his rounds; he thought it was neuralgia, as it was relieved for a time by phenacetin. It gradually extended, however, down both sciatic regions, but he did not believe it to be a sciatica because, he declares, the sign of Lesègue was absent. In July the pains became of a shooting character from time to time, remitting at intervals. About this time, too, he noticed an absence of his patellar reflexes; but he states that he is not sure that they were ever present. He began to be unable to finish his operations on account of tire of the back; and in consequence he began to lessen the amount of his work. Later, climbing a slope or staircase became difficult to him, and he became discouraged, apprehensive, and dreaded having to do his work. His micturition, too, became difficult, and he could abstain for a long time; while sexually he was less potent.

To this state was added the fear of making a mistake in his practice, as his hand now trembled, and the feeling that he might not be able to finish an operation after beginning it. He began to do less and less work, but did not improve; and in September a peculiar sensation began over the buttocks, mainly over the left side. He described it as a feeling that the skin and subcutaneous tissue felt as if they were a leather cushion, so numb were they. The feeling extended into the adductor regions and perineum; and on one occasion during a climb he could hardly believe that the

latter region had not undergone laceration, so intense was the sensation of perineal tear.

He has noticed no other failure of his powers, bodily or psychic, believing that even his memory is intact.

Physical Examination.—Muscular power is strong, but unsteadily used, especially around the left orbit when he attempts to close the right eye alone and around the nose when he grimaces. He cannot draw the mouth to the right; the lips tremble slightly, but the tongue does not. Speech is slightly tremulous, although the test phrases are said with only an occasional drop of a letter or syllable. Muscular co-ordination is slightly inaccurate, especially on the left side.

The diadocokinesis is impaired in the left arm. There is no diplopia at less than one foot distant; but at four feet or more he can see two distinct images when looking to either side. Towards the left, when the right eye is covered, the image which disappears is that situated superiorly and to the right; when the left eye is covered, the lower and left image disappears. The left eye is unsteady during this. When he looks to the right, the images are on the same level; and the right image disappears when the right eye is covered, and *vice versa*. The two images are equally distinct in all cases. The *sensibility* was normal with the exception of a defective appreciation of passive position in the left toe; but a tendency to misinterpretation was manifested, especially on the left side.

Reflexes.—Both patellar and Achilles absent; radial and olecranon present though dull; bulbocavernosus absent. The cutaneous reflexes were active, with the exception of the left cremasteric and the plantars; of these the left was immobile, and the right in feeble flexion. The pupils are widely dilated but not irregular, and react well to light, but less well to accommodation. They dilate well to the Piltz test, recontracting quickly. The fundus oculi presents a grey papilla, and on the left side, granular old chorioidal pigmentation; while below the papilla and to the right is a round area of greyness.

EXAMINATION OF THE PSYCHIC FUNCTIONS.—*Memory.*—Although he believes it to be good, he fails to remember five letters in sequence, and is very uncertain in his replies and is quite con-

scious of this. Tested with figures, he generally fails to remember a sequence of six, and is equally aware of the uncertainty he shows. Tested the following day, he did better, being uncertain at six figures and less uncertain with seven letters. With Winch's test of reproducing twelve letters in position, he scored only 50 per cent. after thirty seconds were allowed for memorizing; but when given one minute he was nearly correct. The estimate is made by counting three points for each letter correctly placed, two for each letter misplaced one place, and one point for each letter two places wrong. His recognition of words gave an error of 14 per cent. Lines of different length were recognized well. Memory of phrases was good when the story was simple; but when he tried to remember a series of abstractions, he did so very badly, scoring less than 50 per cent.; but he excused himself on the score of "trying to remember the words."

Perception.—Recognition of pictures was accurate; but he did not notice the differences of dress which the same individual sometimes showed. With the series of test cards depicting physically impossible phenomena he was quite successful.

Calculation.—In the test of taking seven from a hundred and continuing to take it from the remainder, he consumed one and a quarter minutes on an average, and failed to perform it correctly, sometimes making two errors, and being often very dull and hesitating in replying.

Generalization was good when he understood, which was not always the case. A series of association tests was undertaken; but from the example given, it will be seen that no conclusion could be derived, so that I need not give them in full. Of the more simple replies the following gave prolonged reaction times: "Strong," "vegetables," "Indians," "seeing a train," "hammer," "lead." As these out of over a hundred words did not convey any indication, I abandoned the test. They responded to the words: "Fifty-pound weight," "market place," "Indian clubs," "train," "iron," and "wet paint," respectively.

When it was explained that I wished ideas rather than mere definitions, his answers were as follows. (The smaller number is the time in seconds before the patient commenced to write after hearing the test word, the larger number is that of the duration of his reply.)

"Cow." (4) (38) "Seeing an old man milking a cow in a barn on the home farm."

"Omnibus." (2) (40) "Seeing the omnibus going up Broad Street, Philadelphia."

"Piano." (4) (45) "Seeing a young lady at the piano in the dining room at hotel last night."

"Rushing water." (4) (37) "Seeing the Potomac river running over the boulders in its bed."

"Nettles." (3) (55) "Coming in contact with a nettle bush in the woods at our country home."

"Velvet." (2) (60) "Seeing a lady on the street car this morning with green suit."

"Strawberries." (10) (50) "Seeing a strawberry patch with the fruit on and a great many people picking them."

"Vinegar." (3) (30) "Being in vinegar cellar and seeing barrels of it."

"Cramps." (2) (20) "Thinking of pain I had in my abdomen night before last."

"Mowing machine." (9) (40) "Being on a mowing machine myself and having a runaway by getting into hornets' nest."

"Factory." (2) (25) "Passing a chair factory in the town at quitting time."

"Train whistle." (3) (29) "Seeing one train approaching another."

"Wet paint." (3) (22) "Having it on my hands."

"Thorn tree." (3) (13) "Seeing a tree covered with its ripe berries."

"Fish." (3) (23) "The fish I had for breakfast, a pan fish."

"Fifty-pound weight." (5) (55) "Seeing a man raising a dumb-bell of that weight."

"Wind." (3) (30) "Seeing the trees bending in a storm."

I made a diagnosis of taboparalysis, and believed it to be luetic; for a clinician should never forget that the anamnesis of the patient may be inaccurate on account of his unwillingness to face an unpleasant situation, and that without wishing to be deliberately untruthful certain people find it very easy to suppress unpleasant memories and even fail to perceive the circumstances which they believe disadvantageous. These considerations are particularly

applicable in such a disease as syphilis or such a condition as insanity in the family.

The reasons for the diagnosis of tabes were the pains and paræsthesiæ of radicular character, the diminished sense of position in the left toes, the absence of the Achilles, patellar, and bulbo-cavernosus reflexes, and the diplopia, as well as the slight inco-ordination exhibited. The pathogenesis and radicular distribution of tabetic symptoms have recently been discussed by the author² and need not here be enlarged upon.

For the diagnosis of dementia paralytica, the most significant symptoms were the definite incapacity of the memory, the inaccuracy of calculation, and the slowness and difficulty of understanding the data, which caused the difficulty of generalization. Definite gaps like this are very significant of organic defects of the brain; whereas a general intoxicative process is more apt to give rise to a mental confusion extending to all the faculties. An arterial sclerosis localized within certain areas might produce such a syndrome as this patient presented; but it is improbable that it would have been accompanied by the same erethism of the nervous system; and, moreover, the meningeal process which was the source of his tabetic symptoms is by far the most usual cause of the kind of dementia he showed. Pathologically, chronic meningo-encephalitis differs from tabes dorsalis only by its locality and the sequences thereby conditioned.

The treatment I recommended was that he should proceed to Florida for the winter; take much rest in the open air, alternating with short periods of active movement; apply hydrotherapy in the form of warm baths to obtain their tranquillizing effects (their use was not to exceed twice a week); to massage the eyes, with a view of diminishing mydriasis by stimulating pupillary contractions; to urinate every two hours during the day and when he awoke in the night; to take a nourishing diet relatively poor in purins; and to employ intramuscular injections of hydrargyrum every seven days. By contrast with my next case, he failed to follow this treatment, his want of will making him an easy victim to the vain promises of an electrotherapist. Diagnostic precision was thus rendered fruitless, as, of course, he has not improved.

The second case was also one of general paralysis.

CASE II.—The patient was a clerk aged 40, referred to me by Dr. Lewis L. Taylor, May 6, 1908, complaining of a nervous breakdown following “indigestion” of five years’ duration.

Family History.—Good, though he has a psychasthenic brother, also a patient, but able not only to accomplish his work in a government department but to perform literary work of a special kind in his spare time.

Previous History.—He has smoked four cigars or more a day, and chews tobacco, but takes alcohol only about twice a month. He has taken no coffee for six months, as he found it made him much more “nervous.” He enjoys his food, and eats meat two or three times daily. He is a single man living with his parents; he believes this state more “comfortable.” He is of regular habits, and retires at ten o’clock P.M. There has been no sexual excess.

Twenty years ago he had a chancre which lasted a month. He does not remember the details of the illness except that the sore exuded slightly, and that he noticed no eruption, and that he was out of sorts for some time and received medical treatment. With the exception of an orchitis accompanying mumps twenty years ago, which was painful from time to time, he has had no definite complaint, never having had typhoid, malaria, influenza, or gonorrhœa.

Present Illness.—Nine years ago after eating a raw turnip he became sick, and since then has suffered with “misery in the stomach and all over.” He has felt “useless and depressed most of the time” and “almost as if he wanted to die.” Accessions of a “desperate want to run away from it” have occurred; but he never does go. For the last two years, he has had sensations of dyspnœa and sinking feelings in the epigastrium; these occur suddenly and seem independent of external cause. There have been no choking sensations. Some nights the bowels would act two or three times, with discomfort and sometimes pain; there was no mucus, but sometimes diarrhœa; these symptoms have ameliorated lately. There has been no difficulty or precipitancy of micturition, though he has sometimes experienced a burning sensation in the urethra. In the chest he has had “light” feelings, and also pain and thumping of the heart. There has been a jerking pain in the right groin.

He has had nervous chills in which he trembles, shakes, and feels

"no good." For two or three years his voice has been tremulous, especially in public speaking. He states that he suffered from stammer as a boy, but not afterwards. At times he not only feels like crying, but actually does so, about imaginary troubles as well as real ones. He states that he is never jovial. A year and a half ago he gave up banking work because he felt it too much of an effort, though he declares that he made no errors. He feels himself unable to resume this work, and has been soliciting for an insurance company, as this takes him outside. In the last six months he has gained ten pounds in weight. He has noticed no loss of memory; but he declares it was never good, as he depended upon a book.

Physical Examination.—Breath foul; thick crown of fur on tongue; stomach not markedly dilated; abdomen somewhat distended; no abnormalities of circulatory, respiratory, or urinary systems.

Motility.—Deficient in the left corrugator supercilii and orbicularis palpebrarum in frowning. Trembling of left cheek during sneering, trembling of tongue when deviated. On extending the arms, the right fingers tremble more than do the left. Against resistance, adduction of the right thigh is imperfect.

Sensibility.—Normal.

Reflexes.—Those of the tendons were all exaggerated. The radial and maxillary were equal on the two sides. The right triceps was more active than that of the left; while the liveliness of the patellar, Achilles, and deltoid reflexes was the greater on the left side, the patellar reflex being quite exaggerated. Of the cutaneous reflexes, the abdominal were diminished. On stroking the right sole, the outer toes extended, while the great toe was immobile. On stroking the left sole the toes remained immobile, while the whole foot adducted. With the Oppenheim and Gordon methods no reaction occurred. A curious indication of exaggerated overflow of nerve impulse was afforded by the contralateral extension jerk of the foot upon tapping the opposite tendo Achillis. In the case of the left foot, this was accompanied by adduction, and the extension was more violent and easily produced. In the effort to arise from the recumbent posture, the left heel leaves the floor slightly.

The pupils are moderately dilated, equal, not irregular, and react well both to light and accommodation. Around the iris is an arcus senilis.

PSYCHIC FUNCTIONS.—Memory.—No deficiency is perceptible in the recognition of lines, positions, portraits. He can remember seven letters, and eight figures; and with Winch's test is fully up to normal. He recognized words accurately, and the memory of phrases was not impaired.

Perception.—He readily perceived the absurdities in the test pictures.

Calculation.—Continuous subtraction of seven from a hundred: 93, 86, 71, 64, 57, 50, 43, 36, 29, 22, 15, 9, 1. Time occupied, forty seconds. Second test correct to 29; then 22, 14, 7. He hesitated from time to time and was very slow. He then performed the test correctly twice. Addition was performed correctly and rapidly. Division was incorrect, and he tired quickly while doing it.

Generalization.—Seemed quite good, and insight unimpaired. No association tests undertaken.

It should be added that his speech was slow and rather thick, but showed no elisions, syllabic repetitions, nor hesitancy; and that the test-phrases were accurately repeated, with the exception of "she cooks cup custard." The examination was discontinued owing to his fatigue; and he was immediately placed under treatment similar to that in the foregoing case, with the addition of abdominal massage and a richly alkaline diet, poor in nitrogen, and practically free from purins.

The examination was resumed on May 9, on which occasion he could remember eight letters and seven figures, and performed the "seven from a hundred" test correctly in forty seconds; but when attempting it in thirty seconds he made the following errors: 58, 51, 43, 36, 29, 21, etc. Out of eight nonsense syllables, he could reproduce six. In dictation of about forty words he omitted only one letter, the first "t" in "representatives." There were, however, several errors of spelling, to which I could not attribute significance.

On May 19 the letter memory was as before; the "seven from a hundred" test was performed correctly in forty seconds; the reflexes were less lively; and he looked and felt better.

Every second day during this period he had received $\frac{1}{12}$ gr. hydrarg. perchlor. in ten-minim doses in normal saline solution, as he dreaded the pain after injections of metallic mercury. The expense of residing in Washington being too great for him, I ventured an

injection of grey oil before he returned to the country, as, for personal reasons, he was unwilling that anyone at home should know of his condition. However, as he suffered much pain, it was arranged that a pharmacist friend of his should nurse him, and give massage and the injections of perchloride of mercury. I instructed him in the asepsis required, but within a short time two painful swellings arose; and the patient returned to the neighborhood to resume treatment by me personally.

On May 27 he was feeling much better. The letter memory was normal. A sequence of ideas was directly reproduced without hesitation or difficulty. The "seven from a hundred subtraction" was accurate, steady, and rapid. However, the mouth still trembled; but the tongue did so only when deviated to the left. The reflexes were still too lively, that of the left patella exceeded that of the right, that of the right radial exceeded the left, while the others were equal on both sides. The speech was still imperfect. The tongue was cleaner, but the breath was still foul.

The first mercurial course was completed on June 26, when the breath had little odor, the tongue was cleaner, he digested and felt much better. He wished to go to a mountain spring resort. I therefore selected one for him. On this occasion, his pronunciation showed no defect, the trembling of the lips was much less marked; but he was still incapable of frowning, and had very little power to raise the eyebrows. He stated that he could never close the right eye alone. The previous memory tests were performed perfectly. The subtraction is done correctly and fairly rapidly, but with pauses at 86, 72, 44. He mentally divided 735 by 39, answering after deliberation, "about 18 times." After a few moments' consideration he saw that "a man could not marry his widow's niece."

October 21, after his return from the mountains, he felt still better and was able to do office work without tiring or becoming irritable if he did not prolong it beyond two to three hours at a time. The defects of movement still persisted, though there was less trembling and the reflexes were no longer exaggerated. He has noticed what he calls a "nervous flush" on the backs of the hands when a vivid impression occurs. Sometimes while in bed he has a tired sensation in the feet, which is relieved by a few minutes' standing or walking; it may occur several times in the same night. He

declares that his pupils became dilated widely on account of reading figures aloud for some days; they were no longer so dilated when I examined him. A mercurial course of gray oil once weekly was resumed. The letter memory had diminished, he usually failed at seven with one or more letters; with figures he usually failed at eight; with the twelve letter position test of Winch, there was no defect, and the "seven from a hundred" test was correct in 30 seconds. Three "Irish bulls" were quickly detected.

November 24, he no longer complains of pain after the injections. He has made a business journey without fatigue, although it lasted two days and a night, during which he did not sleep on account of changing trains and discomfort. He had to come through a wood alone at night and without a revolver, and did so without any fear, a feat he declares he could not have done formerly. After the trip he was neither worried nor unduly tired, and it has caused no exaggeration of the reflexes. The abdominal reflexes are absent, and the right cremasteric reflex is very faint. On stroking the left sole, the toes remained immobile, and there was slight adduction of the left foot. On stroking the right sole the four outer toes extended, the great toe not moving. The memory now shows no deficiency; he recalls seven letters and eight figures.

The symptoms in the case were quite *fruste* and none of the signs pathognomonic. I had to depend upon the dissimilarity of the reflexes on the two sides and the relative increase of those of the tendons and diminution of those under the skin, along with the trembling of the cheek and tongue and deficiency of unilateral brow movements, as well as general erethism.⁸ These signs are insufficient even for a diagnosis of so-called parasyphilis. But though the memory was apparently intact and both perception and insight were quite clear, his difficulty, hesitancy, and inaccuracy in subtraction and division indicate in a man of his training a serious gap in the intellectual faculties. The improvement of these defects under mercurial treatment while the physical abnormalities remained, with the exception of the exaggerated reflexes and erethism, indicates their syphilitic origin. This is corroborated by the relapse towards the end of four months' intermission of treatment. The tired sensation in the feet at night is indicative of a toxic paræsthesia affecting the roots. The pupil dilatation after the fatigue of long reading

may have a similar source. Slight diminution of memory was equally indicative of need for further treatment.

The accession of miserable depressed states, with trembling, excitability, and lachrymosity, along with the intellectual defect, the inequality in the reflexes, and the trembling and lack of power in the face, are I believe sufficient to constitute a diagnosis² of the neurastheniform prodromata of dementia paralytica. My belief that this is a syphilitic rather than a parasymphilitic disease is strengthened by the benefit he has received apparently from mercurial treatment conducted by intramuscular injection, and combined with very careful hygiene, the *régime antitoxique végétarien* so much lauded by French physicians.

The prognosis which I gave to the friends as guarded has now become more hopeful, and I trust that I may be permitted to report the case further after some years have elapsed.

CASE III.—The third case was seen with Dr. Main of Washington at the suggestion of Dr. Prentiss of that city, Oct. 30, 1908. He was a man of 54, a farmer, who had been in a "neurasthenic state" since the spring, for which rest, change, and a sea voyage had been prescribed without more than temporary benefit. He complained of insomnia, general nervousness, and a state of suffering, incapacity, and irritability.

The *family history* was negative.

Previous History.—His wife is living and healthy. There were no children or miscarriages. He denies syphilis; but some years ago had typhoid fever, during which he lost his hair, which has now regrown. When closely questioned he recollects having been subject to spells of depression every few years, and also to periods of activity and energy, which he strikingly describes as "wanting to get at it." He has noticed no change in his speech, which is a little dragging.

Present State.—When seen by me he appeared neither depressed, shaky, nor apprehensive, though the previous day he had felt perturbed and despairing of recovery. His chief trouble is insomnia.

Physical Examination.—In spite of the cold of the room, the window having been widely open, when he is stripped for examination perspiration appears in both axillæ and down the internal border of the left arm; later some drops appeared on the left leg. This want of correspondence of the sudorific function with the

stimulus of heat and the local if not segmental distribution of the anomaly indicates a serious perturbation of the autonomic nervous system. The localization of the disturbance moreover signifies organic involvement rather than general toxæmia.

Motility.—Facial, tongue, and ocular movements are steady. The muscular power is strong, but the movements are slightly incoordinate, especially in the right hand; and when the arms are extended there is a rhythmical tremor which becomes irregular during the maintenance of the attitude. The diadokokinesis is hardly impaired. The platysma trembles when the mouth is pulled to the right.

Sensibility is intact except that in the left lower extremity. L. V. and S. I. 2 are insensitive to the diapason. A similar anæsthesia exists over the distribution of the posterior primary divisions over the sacrum. This shades off above as far as the second lumbar spine, where the vibrations are normally perceived.

Reflexes.—The pupils contract both to light and accommodation, but in each case tend to redilate while still stimulated. The left pupil is slightly irregular. On the right side the radial reflex is active and that of the triceps is feeble. On the left side the radial reflex is feeble and that of the triceps is active. The Achilles jerks are equal. The left knee-jerk is exaggerated, the right is diminished. Both abdominal reflexes are diminished, especially the left, which is almost absent. The cremasteric reflexes are very faint and sometimes crossed. On stroking the sole of the left foot the toes flex and the tensor fasciæ femoris contracts. When so stroked the right foot flexes and flexion of the toes is scarcely appreciable, though the tensor fasciæ femoris contracts actively; there is no response with the Oppenheim and Gordon methods.

Speech.—He says there has been no change; but it is drawling, slithering, and there is now and then a catch in a word or letter and sometimes a repetition of such commencing consonants as *c* and *d* and such words as “not” and “denied.” The test phrases are all well said. The writing, for an educated man, son of a physician, is rather irregular and unpunctuated.

PSYCHIC EXAMINATION.—*Memory*.—Fails consistently to remember eight figures, sometimes fails with seven, can remember six letters, but not seven. With Winch’s twelve letter position test,

after an interval of forty seconds he scored thirty; but when sixty seconds elapsed his scores averaged only twenty-one out of a possible thirty-six. Memory for connected narrative was not impaired and dictation was accurate.

Calculation.—The “seven from a hundred” test required eighty-five seconds, and was correct until 16, when he answered “eight” on two occasions. On the first attempt after reaching 79 he said 62; and although hesitating and apparently confused, he was conscious of a lapse, and recommenced. The second test was completed in forty seconds.

Generalization and judgment were not tested from lack of time, but insight seemed lacking, for in his manner he portrayed no consciousness of the gravity of his situation, during my examination at least, although Dr. Main tells me that he is often much discouraged by his illness, and the patient himself informed me that he feels a lack of interest, which begins with a peculiar feeling in the abdomen as if everything there were in motion, a twitching, like the sensation occurring after a debauch; this is followed by a sinking feeling and unhappiness.

He was advised a *régime* similar to that of the preceding cases; and he forthwith began to take one-third of a grain of hydrargyri succinimidum every other day. He began to sleep much better, and to be less irritable and nervous. At my wish the cerebrospinal fluid was examined, and was reported to be clear and free from cellular elements after a single examination.

On November 13 the perception was tested by pictures I use for the purpose: each of them contains an impossible conjunction, such as smoke and trees blowing in different directions at the same time, a horse drawing a load uphill with a slackened chain, shadows in wrong positions, a person looking out of a window situated in a chimney stack from which smoke is issuing, a man watering flowers with a broken hose—all very glaring faults. Although he remarked upon the occasional and irrelevant peculiarity of the drawings, in no instance did he detect the absurdity portrayed. “Seven from a hundred” test: mistakes at 51—43 and 29—21; time, thirty seconds. Division also was inaccurate.

His recognition of lengths was only one millimetre in error, and this can hardly be called abnormal. After five minutes’ study,

he remembered perfectly twelve nonsense syllables, and reproduced them in order. He was only inaccurate in two places when he endeavored to replace in order eight words seen one minute before; with a second set of eight, only two words were correctly placed, although he believed it the more exact reproduction of the two. From a list of twenty words, he picked out eight previously seen, making only one error of insertion, and being uncertain of another word. Neither of these tests indicates serious abnormality. Later, in taking seven from a hundred, he was correct in thirty-five seconds, though he hesitated a little; he then repeated the test without hesitation in twenty-five seconds. The speech showed now an occasional doubling of a labial, a substitution with rapid correction, such as "expedexpectation," and the omission of a word in a difficult phrase as, for example, "annoys" from "what noise annoys a noisy oyster most."

I could not elicit the arm reflexes, and found that the right patellar reflex responded only on reinforcement. The right pupil reflex was quite sluggish, especially on the nasal side. Examination with a lens showed irregularities of both pupils, especially the left. There is trembling of the nasolabial folds, palate, and right eyebrows when the mouth is open. There is no ataxia.

Reexamined on December 21: no trembling of face or hands, even when movements were performed; no ataxia; when eyes were closed, the two fore-fingers could be brought together almost exactly. The contraction of the pupil when exposed to light was maintained now over ten seconds; the contour, however, is still irregular. The patellar reflexes are over-active, especially the left; the left Achilles reflex responds more actively than the right; the right plantar reflex is absent, while on the left side the lesser toes extend when the sole is stroked; the cremaster reflexes are sluggish, but the abdominal are present. The anaesthesia over the left foot shades off above and over the patella; the outside of the foot is hypoaesthetic to wool. The rest of the sensibility is as before.

His memory has improved slightly, for he easily reproduces eight figures and can always remember seven letters, and sometimes even eight. He made the subtraction of seven from a hundred in twenty-five seconds, the first time making errors at forty-four and twenty-seven; but he knew he was wrong, and himself detected

the errors after finishing the test; he then performed it correctly in the same time. He was fully up to the normal on the average of remembering the position of twelve arbitrary letters, for he averaged thirty-four of a possible thirty-six. In memorizing twelve nonsense syllables he omitted only three and made one error. The test-phrases were repeated correctly; and on reading, the reduplication of a syllable was rare. In remembering the order of a series of twelve words, he made only two inversions.

Since then he has been at work on his farm, and his physician reports that he has not felt so well or been so strong for years. He has been eating well and has gained weight, while his mental state and disposition appear to his neighbors quite normal. While this is probably the case, I believe that another psychometric examination would reveal some small gaps, in the intelligence at least. Of course, the final prognosis of this and the other case is still impossible, and only time can make it certain with our present limited knowledge of quaternary syphilis. I hope, however, that the publication of these cases will induce others to report similar ones.

I had no difficulty in making a diagnosis of general paralysis of the insane.³ The physical symptoms pointed strongly towards a syphilitic (parasymphilitic) affection of the central nervous system. Pupillary irregularity, failure to maintain reflex impressions, and segmental sluggishness are almost pathognomonic. When lateral inequalities of the reflexes occur without symptoms indicative of peripheral neuritis or muscle involvement, one must strongly suspect spinal-root disease; and the sensory loss in L. V. and S. I. 2 strongly corroborates this. The trembling of the hands and face are important indices of the extensiveness of the morbid process; and the speech defect is suspicious of the disease in question.

But it is not until we examine the mental functions that the diagnosis is assured, and it is by psychometric methods, and by them only, that this case shows the gross failure of perception demonstrated by the tests with the pictures of impossible conjunctions, the quantitative diminution of memory, and the errors of calculation, small and occasional though the last are.

It will thus be seen that the tests employed are exceedingly simple and need no special skill in their application except that required to avoid suggestioning the patient when he requires prompt-

ing to make it certain that he comprehends the demand of the test. It is true that they require patience and consume time; but it is doubtful whether they take longer than the more usual desultory talk; and even though they did take longer, they have the merit of leading to data which can be expressed definitely, as against the mere report of the examiner's impression, which is the statement usually made. The readers cannot bring into comparison with their own cases the terms used by another observer, whose personal equation necessarily deprives of all precision such quantitative estimates as markedly, considerably, poorly, feebly, etc. (It will be observed that this aim was by no means attained in every respect in these cases.)

This method no more converts the examination into a mechanical process, and no more negatives the common-sense judgment of the observer than does the use of the hæmatocytometer and sphygmomanometer obviate the employment of skill and knowledge and an avoidance of the fallacies of application and interpretation in the laboratory of general medicine. As a matter of fact, the patient who is essaying the tests affords a better clinical picture as regards his general conduct than he would do when this interview is chiefly conversational. While adapting himself to the tests, he reveals numerous little mannerisms which might otherwise not present themselves at all; for he is absorbed in his task while the examiner may watch him at leisure.

It may be complained that the method I have used leaves the examination sadly incomplete; but it must be remembered that practical applicability is the chief aim of my paper; and accordingly I have purposely avoided the discussion of tests which require apparatus, such as the measure of the attention by the revolving spiral or by the moving shutter, employed by experimental psychologists; the measure of fatiguability by Mosso's ergograph, and its adaptation by Mlle. Ioteyko in combination with a myograph in an attempt to analyse the fatigue curve; and the measure of the affectivity (if it so proves) by the galvanometric apparatus of Veraguth. Nor have I by any means exhausted all the available tests.⁴

That we are not yet even within reach of the measure of the emotions need be no reproach to that which we have already acquired

as regards the intelligence; for we are still very far from being agreed about the organs of emotion, and still further from a knowledge of its mechanism. We do not certainly know the nature of co-enæsthesia, and some indeed even go so far as to deny the existence of organic sensations. For the present, therefore, we must be content to describe emotional changes in the vague terms which need no longer serve to describe the abnormalities of the intelligence.

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³ See Case II in the article on General Paresis by Jelliffe in *International Clinics*, vol. iii, series 18, diagnosed on symptoms even less manifest.

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Pathology

PERITHELIOMA TESTIS

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THE patient, C. W., 32, married, first noticed a slight swelling in the testicle eleven months before operation. It gradually increased in size and was absolutely painless. When first seen at the Sussex County Hospital the right testicle was found to be enlarged to the size of a large duck's egg. The outline was smooth; there was felt a slightly marked groove, running obliquely across the front of the swelling. Above this groove the consistence of the tumor was rather softer and more elastic than below it, but generally speaking, the whole swelling gave the impression of its being solid.

There was no testicular sensation in any part, whatever. There was no thickening of the cord. The skin of the scrotum was not involved. The epididymis could not be differentiated from the rest of the growth. No enlarged abdominal glands could be felt. Although the patient denied syphilis he was given mercury and iodide in considerable doses for a month.

During this time there was no appreciable difference either in size or consistency of the tumor. It was decided therefore to remove it and the operation was performed by Mr. F. J. Paley, the cord being divided close to the internal ring. The patient made a good recovery and was up on the tenth day. On his discharge a few days later there was no sign of secondary growth elsewhere.

LABORATORY REPORT

Sections were made from the soft red area (1) (see Fig. 1) of the specimen (Labtr. No. 3253), from the centrally situated yellowish-white area (2), and from the granular whitish area (3). (1) and (3) enfold the large central area (2) somewhat as the globus major and minor of the epididymis encase the body of the testes. All the growth is within the tunica vaginalis.

The diagram (1) shows peritheliomata of the blood-vessels in an entirely hemorrhagic and necrotic stroma. Stretched over the growth between it and the tunica vaginalis are the lobes of the testes and tubuli seminiferi.

The perithelial cells form the bulk of this part of the growth. Their arrangement is one, a few, or several layers of flattened cells arranged circularly about a central lumen. This is either large or

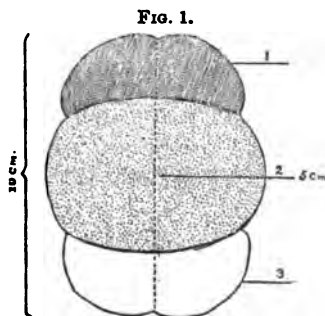


Diagram of tumor of testicle.

again small or contains erythrocytes, or plugs of necrotic endothelial-like cells. Applied to the circularly arranged cells are "palisade-like" layers of cells, three or four deep, or the endothelial cells of the vessels become irregular in their relationship to the axis of the vessel and gradually become placed at more or less right angles or radiate. The cells are polymorphous in shape, being elongated when situated about the vessels; or rounded, with the morphological characters of endothelium; or stellate (myxomatous).

The epithelium of the tubuli seminiferi is degenerated, flattened or atrophic. The vessels appear to be unaffected in the part of the testis examined.

The yellowish-white central area of growth (2) presses upon the body of the testis, which is flattened between it and the tunica

vaginalis. It has a very abundant stroma, which is of spindle or round cells, or is necrotic. The nuclei are flat or round.

The cellular areas are irregularly rounded in shape or bifurcate and give off branches now and again. Near the testicular tissue they exist as small tubules with one or several layers of columnar or cuboidal cells; more distantly they have choked the lumen of the tube and undergone mucoid degeneration and broken down, or again the cell bodies cannot be stained and appear to have undergone oedematous swelling, leaving their outlines as a delicate layer of chromatin. The cuboidal cells are seen then only at the periphery of the cell mass. Other areas are of hyaline or fibrocartilage or fibrous tissue, sometimes of considerable size. One cartilaginous area has a small sprout in which there appears to be a lumen containing some erythrocytes. The whole growth is the seat of hyaline changes in places.

The vessels of the testes stretched over the growth are either unaffected or have collections of small or large round cells about them or again are peritheliomatous.

The whitish granular area (3) is endotheliomatous, that is to say, it is composed of strands of endothelial-like cells, without much lumen formation, in a stroma. There is thus a structural resemblance to carcinoma. The cells of the solid strands, which branch and swell irregularly, have the brilliant appearance described by Lazarus Barlow in stained preparations of endotheliomata. It is due to the chromatin of the nuclei being collected in the centre and periphery and allowing much light through it. The nuclei are rounded, rather large, and the cytoplasm does not stain. Tubule formation is limited. The stroma is in bands, or is very abundant, and freely nucleated, or again is necrotic. The vas deferens is unaffected. There is no evidence of dermoid growth or chorio-epithelioma testis.

Remarks.—1. From the description, the tumor is seen to be a perithelioma and endothelioma of the blood-vessels (angiosarcoma). It would therefore arise in the small branches of the spermatic artery, either as they supply the epididymis, or as they subdivide in the posterior part of the mediastinum testis, behind the rete, or possibly in the vascular lining of the interior of the tunica albuginea before being distributed to the lobes of the testis.

2. There is every probability that the perithelial and endothelial as well as the tubular growth is derived from similar cells to those which are observed to form in other parts of the growth, cartilage and mucoid-cell foci. As the endothelium and blood-vessel walls are derived from mesoblast, such elements are not unlikely to revert to other forms of connective tissue as cartilage or fibrous tissue, under the disturbing influence of tumor formation. On the other hand the presence of such elements as true hyaline and fibro-cartilage may be regarded as evidence of the endothelial and mesoblastic origin of the growth.

3. It appears that there is in addition to a stimulation of proliferative activity, a loss of the guiding influence which normally directs orderly growth. This results in the neoplastic changes of the blood-vessels and permits also the original tendencies of the mesoblast to assert themselves in the endothelioma and to differentiate, as in the embryo, into various forms of connective tissue.

4. There is nothing to support an origin of the growth in the epithelium of any part of the seminal tract (tubules, vasa recta, rete, efferent or excretory ducts), the embryological derivation of which is in part undetermined.

5. It is probable that these growths are usually described as carcinomata, especially when differentiating as in area (3) of diagram.

Prognosis.—This is guarded but not absolutely unfavorable as regards life. In a former case recorded by me under the care of T. H. Ionides, M.B., F.R.C.S.,¹ the patient was operated on in June, 1906, and is to-day alive and well. E. J. Wood describes an endothelial metastasis from a testicular sarcoma.² Sternberg has collected fifteen such cases.³ Krompecher reviews fourteen such cases.⁴ MacCallum records a case of lymphendothelioma testis,⁵ which Teacher regards as teratomatous (chorio-epitheliomatous).⁶

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THE PATHOGENESIS OF SPONTANEOUS CEREBRAL HEMORRHAGE

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THE pathology of cerebral hemorrhage has been for scores of years a fruitful subject of discussion. Chiefly since 1840 there has accumulated an extensive literature, even a brief review of which is beyond the scope of this paper. The monograph of Löwenfeld contains an excellent summary of the various findings previous to the year 1886. His report of seventeen brains is second in extent only to the classical work of Charcot and Bouchard in 1868. Both these studies were made by such methods that instructive comparison between the results thus obtained and the findings detailed in this paper cannot be drawn.

The conclusions of writers as to the actual vascular lesions leading to cerebral hemorrhage are very varied. To each of the three arterial coats has been ascribed the initiative rôle, and in each the nature of the process has been variously interpreted. Since the work of Charcot, miliary aneurysms have been given the leading place in the immediate etiology, but their nature and method of formation has not been satisfactorily determined. That diseased but non-aneurysmal vessel walls rupture has been asserted and denied.

This lack of definite knowledge and consequent conflict of opinions regarding the arterial changes and the aneurysms found in cases of cerebral hemorrhage is largely due to the inadequate methods formerly employed in the microscopic study of these brains. Surely the condition of the various coats of an artery cannot be accurately determined by mounting the entire vessel and examining the inner as they lie beneath the outer layers, the technic employed in many of the reported studies. I have found no report, in recent

years and based on modern technic, of a series of cases sufficiently large to furnish reliable data concerning the question at issue. As such data appeared highly desirable the present study was undertaken. For the material investigated and for confirmation of my work I am indebted to Dr. Ludwig Pick, Prosector of the Friedrichshain Hospital, Berlin. To him I hereby extend my sincere thanks for his many courtesies.

MATERIAL STUDIED

The material on which this paper is based consisted of 31 brains from cases of spontaneous cerebral hemorrhage. As may be seen from the accompanying table, 13 of the subjects were men and 18 were women. This proportion of 58 per cent. of women to 42 per cent. of men is unusual for a series of cases. Monakow quotes Gintrac as finding in his collection of 706 cases, 57.6 per cent. men and 42.4 per cent. women; Falret's 2297 cases included 72.2 per cent. men, 27.8 per cent. women; Kelynack and Bythell's percentages were 77 of men and 23 of women. The proper interpretation of my figures, I believe, is to regard them as a further instance of how a small series of cases may, in the absence of extensive statistics for comparison, be misleading.

The age of 12 of the men and of 14 of the women in my series was known. That of the former group varied from 40 to 77, that of the latter from 34 to 82 years, the average of the men being 60.5, of the women, 59.5 years. By decades the ages were:

30 to 40.....	1, woman.
40 to 50.....	3, men.
50 to 60.....	7, 1 man, 6 women.
60 to 70.....	9, 5 men, 4 women.
70 to 80.....	5, 3 men, 2 women.
80 to 90.....	1, woman.

The four women and one man whose ages were not obtainable were apparently between 60 and 70 years.

Hemorrhage occurred in the left side of the brain in 16 cases, in the right in 12, in both sides in one, in the pons in one; in one there was no visible source of the blood, which was in all the ventricles.

TABLE OF 31 CASES OF CEREBRAL HEMORRHAGE.

No.	Sex	Age	Location of hemorrhage	Vessels of base	Heart	Kidneys
1	M	77	Right internal capsule and lenticular nucleus.....	Moderate atheroma...	Hypertrophy left ventricle...	Intestinal nephritis
2	M	62	Left internal capsule and thalamus.....	Advanced atheroma...	Hypertrophy both ventricles	Intestinal nephritis
3	M	48	Right corpus striatum.....	Moderate atheroma...	Hypertrophy left ventricle...	Paraneurymatous nephritis
4	F	58	Right corpus striatum.....	Advanced atheroma...	Hypertrophy left ventricle...	Diffuse nephritis
5	F	62	Right corpus striatum, thalamus, and pons.....	Advanced atheroma...	Hypertrophy both ventricles	Diffuse nephritis
6	F	51	Left occipital lobe.....	Moderate atheroma...	Hypertrophy both ventricles	Paraneurymatous nephritis
7	M	70	Left corpus striatum and thalamus.....	Moderate atheroma...	Hypertrophy left ventricle...	Paraneurymatous nephritis
8	M	40	Left thalamus; right thalamus and lenticular nucleus.....	Slight atheroma.....	Hypertrophy left ventricle...	Chronic paraneurymatous nephritis
9	F	50	Right parietal lobe and postcentral gyrus.....	Slight atheroma.....	Hypertrophy left ventricle...	Diffuse nephritis
10	F	66?	Left thalamus and lenticular nucleus.....	Slight atheroma.....	Hypertrophy left ventricle...	Slight intestinal nephritis
11	M	58	Right thalamus and peduncle.....	Advanced atheroma...	Hypertrophy left ventricle...	Paraneurymatous nephritis
12	F	50	Left occipital lobe, peduncle, and thalamus.....	Advanced atheroma...	No hypertrophy.....	Diffuse nephritis
13	F	62	Left thalamus and lenticular nucleus.....	Advanced atheroma...	Hypertrophy both ventricles	Paraneurymatous nephritis
14	F	34	Left thalamus, peduncle, and lenticular nucleus.....	Extreme atheroma...	Hypertrophy both ventricles	Paraneurymatous nephritis
15	F	70	Left thalamus and corpus striatum.....	Advanced atheroma...	Hypertrophy left ventricle...	Paraneurymatous nephritis
16	F	66?	Left entire basal ganglia.....	Advanced atheroma...	Hypertrophy both ventricles	Intestinal nephritis
17	M	46	Right corpus striatum.....	No atheroma.....	Hypertrophy left ventricle...	Intestinal nephritis
18	F	56?	Left thalamus.....	Moderate atheroma...	Hypertrophy left ventricle...	Intestinal nephritis
19	M	78	Right entire basal ganglia.....	Advanced atheroma...	Hypertrophy left ventricle...	Intestinal nephritis
20	M	60	Left entire basal ganglia.....	Moderate atheroma...	Hypertrophy left ventricle...	Paraneurymatous nephritis
21	F	58	No evident source.....	No atheroma.....	No hypertrophy.....	Normal
22	M	60	Left thalamus, internal capsule, and lenticular nucleus.....	Slight atheroma...	Hypertrophy left ventricle...	Arteriosclerotic kidney
23	F	60?	Right cerebellum.....	Advanced atheroma...	No hypertrophy.....	Paraneurymatous nephritis
24	F	68	Right thalamus and corpus striatum.....	Moderate atheroma...	Hypertrophy left ventricle...	Paraneurymatous nephritis
25	M	70?	Centre of pons.....	Advanced atheroma...	Hypertrophy left ventricle...	Intestinal nephritis
26	M	66	Right thalamus and posterior part of caudate nucleus.....	Advanced atheroma...	Hypertrophy left ventricle...	Diffuse nephritis
27	M	67	Left corpus striatum.....	Moderate atheroma...	Hypertrophy left ventricle...	Diffuse nephritis
28	F	69	Left corpus striatum.....	Moderate atheroma...	Hypertrophy left ventricle...	Intestinal nephritis
29	F	61	Left thalamus.....	Advanced atheroma...	Hypertrophy left ventricle...	Intestinal nephritis
30	F	71	Left thalamus.....	Slight atheroma.....	Hypertrophy left ventricle...	Intestinal nephritis
31	F	65	Right corpus striatum.....	Moderate atheroma...	No hypertrophy.....	Paraneurymatous nephritis

GROSS APPEARANCE OF THE BRAINS

As in all reported series of cases, the great basal ganglia were the parts of the brain most frequently involved. The corpus striatum was partly or entirely destroyed in 20 instances, the thalamus in 19, a cerebral peduncle in 3, the pons in one, an occipital lobe in 2, a parietal lobe in 2, and the cerebellum in one. The degree of tissue destruction ranged from a circumscribed area one or two centimetres in diameter to the almost entire disintegration of the basal ganglia of a hemisphere. In 27 of the 31 cases the hemorrhage had ruptured into a lateral ventricle and one or several of the ventricles were filled with fluid or partly clotted blood.

The walls of the hemorrhagic foci were formed by irregular surfaces of brain tissue, extensively torn and jagged in some instances, in which were embedded masses of blood; at many points were exposed vessels. On the latter, or on those made visible later by maceration, were found in 20 cases macroscopic aneurysms. These formations varied in number from 2 to 20 in each specimen, a large majority of the brains showing less than 10 and many less than 5, each. They were globular or fusiform masses from 0.5 to 4 millimetres in diameter (Fig. 1). A few were saccular formations projecting from the side of a vessel, but the great majority were uniform swellings with the vessel as the central axis; occasionally one appeared as a terminal bulbous enlargement. They were without exception dark red in color and of firm consistence.

In addition to these unruptured aneurysms there were found in 4 cases ruptured sacs varying from 1.5 to 8 millimetres in diameter. Two of the 5 specimens observed were in the form of relatively small openings in the periphery of an aneurysm (Fig. 2); the remaining three, which were larger, were only segments of empty shells, the remainder of the sac evidently having been carried away during the disruption of the tissues. In one case such a fragment of sac was visible in the fresh specimen and later a second ruptured aneurysm was found in a macerated portion of the same brain. Vessels leading to these ruptured sacs were demonstrable in only two instances.

GENERAL MICROSCOPIC APPEARANCES OF THE TISSUES STUDIED

A routine microscopic study was made of 20 of the 31 brains. The organs were first examined in the fresh state to determine the

FIG. 1.



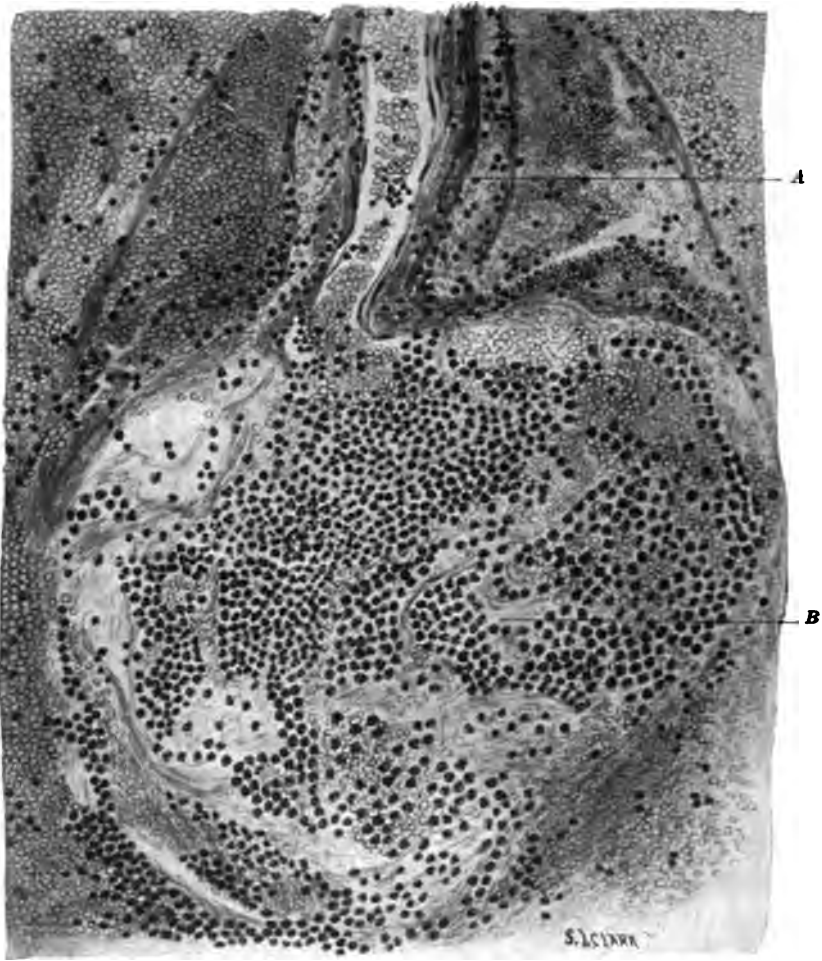
Macroscopic aneurysms assembled from a number of the brains studied. Natural size.

FIG. 2.



CASE XII.—Vessel bearing a ruptured aneurysm. Two diameters.

FIG. 3.



CASE I.—Type of aneurysms found in sections of tissue. *A.* Vessel wall showing on the left side pronounced degenerative changes. The adventitia on both sides is split and elevated by blood. *B.* False aneurysm with its content of red cells, leucocytes, and fibrin. (B. & L., Oc. I, Obj. $\frac{3}{4}$.)

presence or absence of macroscopic vessel changes, especially of aneurysm formation. Numerous small pieces of the lacerated, pulpy portion bordering the hemorrhage were then removed and macerated in water to permit further search for aneurysms. The remainder of the brain was placed for two or three days in 10 per cent. formalin for preliminary hardening and then cut into thin slabs by numerous transverse vertical incisions. From these slabs of each brain were then taken from different points, bordering or at some distance from the hemorrhagic focus, six to ten blocks of tissue, which after further fixation, hardening, and clearing were embedded, the larger in celloidin, the smaller in paraffin. The remaining 11 brains, after isolated aneurysms from three of them had been removed for sectioning, were macerated and examined only as gross specimens.

Owing to the great amount of material collected, serial sections, except of isolated aneurysmal vessels or of occasional blocks, were not attempted. The celloidin blocks, however, which included more than two-thirds of the material, were entirely sectioned; the sections not at once mounted in the usual way were examined after they had been stained by hæmatoxylin and in this way many more were selected for permanent mounting. The routine stains employed were hæmatoxylin with the addition of eosin or Van Gieson, and Weigert's stain for elastic tissue. In addition, sections were stained by orcein, carmine, Weigert's stain for fibrin, osmic acid, and by methyl violet for the detection of amyloid.

As regards their general microscopic appearances, different brains in the series show differences in degree rather than in kind. In sections from all are few or many areas of hemorrhage varying from 50 or 100 microns to several millimetres, occasionally over a centimetre, in diameter. In one extreme case, entire sections are composed largely of medium-sized areas of hemorrhage that are at many points almost confluent. Most of these blood collections are in some portion of their extent in demonstrable relation to vessels, small or large. In the majority of instances the blood surrounds the vessel in an eccentric zone. In most of the smaller areas the blood is within the perivascular lymph-space only; in some of these and in all of the larger it has also invaded the cerebral tissue.

MICROSCOPIC CHANGES IN THE INTRACEREBRAL VESSELS

The microscopic findings in the intracerebral blood-vessels, though exhibiting differences, are essentially the same in all the brains, or can be easily grouped. To avoid the frequent repetition that would occur if they were taken case by case, I shall give a summary of the lesions by describing, (a) the intima; (b) the media; (c) the adventitia; (d) aneurysms; (e) the formation of aneurysms; (f) the actual source of hemorrhage.

a. *Changes in the Intima.*—The description here given applies particularly to the smaller arteries, though some of the medium-sized and larger show pronounced changes. The endothelial cells at points show proliferation. This in some vessels has resulted in new tissue formation, producing a high grade of obliterative endarteritis, though the pure type of this lesion, without regressive changes in the new tissue, is not of great frequency. Granular and vacuolar degeneration of the endothelium is also present in some vessels, and in many there are extensive areas where this layer is almost entirely lacking; some of the cells are strewn about in the blood-content of the vessel, others, judging from the condition of those still present, having entirely disintegrated. At points the endothelial tube is slightly raised from the connective tissue beneath and a few red cells or leucocytes are between them. In other vessels the endothelium is fairly well preserved, even in cases where it with the remainder of the intima is involved in pronounced general changes.

In many specimens the intima, including the elastica interna, shows extensive thickening and degeneration. For example, in sections from Case IV, an artery of 0.1 millimetre outside diameter is seen for some distance in longitudinal section. At various points, in some for considerable length, the elastica is split into two or three principal and several thinner layers with degenerated cells or granular *débris* between. At one point the two outer layers are 26 microns apart, in the included space being a few cell-nuclei surrounded by a mass of vacuole-containing granular *débris* in which protoplasmic outlines are nowhere discernible. The narrower bands of the elastic tissue also show disintegrative changes.

Splitting of the elastica interna into several or many layers with more or less extensive fragmentation accompanying it, is a

PLATE II.

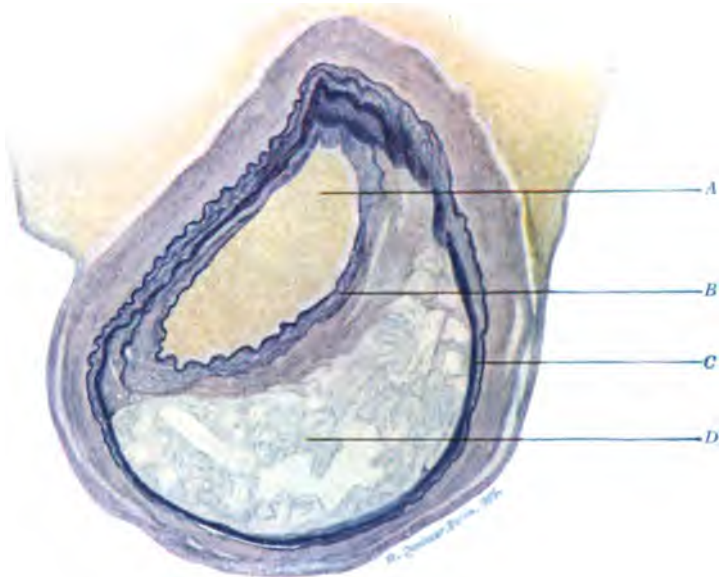


FIG. 4. CASE II.—Splitting and degeneration of elastica of cerebral artery. *A*, lumen of vessel; *B* and *C*, inner and outer layers of split elastica which are here widely separated; *D*, granular debris between the layers of elastica. (Leitz Oc. I, Obj. 5.)

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prominent feature of the intimal changes in all the brains studied. In sections from Case II the elastica of a vessel, which here has a lumen of 0.09 millimetre, in cross-section, shows separation at points into four, for the most part into three, layers. The innermost layer holds essentially the same relation to the vessel lumen as in normal vessels, while for four-fifths the circumference the two outer layers form a somewhat frayed and less deeply stained band which is at the widest point 0.15 mm. from the inner layer (Fig. 4). The space between these widely separated layers of elastica is for the most part occupied by a granular, mesh-like material, poorly stained, in which are many small, almost circular spaces presenting the appearance of fat droplets. A narrow rim of tissue not entirely degenerated is on the outer border of the inner layer, separating it from the granular material described. In this substance and also between some of the layers of the elastica where four are present, are numerous granules or small masses of brownish pigment. This splitting and degeneration of the elastica causes to some extent distention of the vessel, but is largely at the expense of the lumen, which is shown in other sections to be 0.24 mm. in diameter. In another section from this same case a vessel of 0.09 mm. lumen, in longitudinal section, shows splitting of the elastica for some distance with an almost clear space between the parts and with pronounced bulging outward of the outer layer.

Of special value as bearing upon (1) priority in involvement of the coats of these vessels, and (2) the pathogenesis of aneurysms, is an intimal lesion found in many of these brains. This lesion is rupture of the intima with consequent passing of blood beneath that structure and dissecting for a variable distance between the elastica interna and the media.

This lesion of the intima is well shown in sections from Case VII. In a vessel of 0.18 mm. lumen, cut diagonally, the intima for a distance of 0.28 mm. is separated from the media and the intervening space is almost entirely filled by blood. At the widest point the intima is elevated from the media a distance of 78 microns, extending into the lumen of the vessel almost half the width of the latter. This specimen does not show the point of rupture of the intima, but for some distance this layer is a swollen, granular, or almost homogeneous material in which throughout its entire width

are scattered or thickly placed red cells. The endothelium is absent from almost the entire vessel wall, some of the cells being free in the lumen among the erythrocytes. The elastica at other points is swollen, granular or hyaline in appearance, and occasionally slightly separated from the media; no blood-cells are in these small spaces. The media under the dissected intima is with the exception of one or two points intact. At one place are degenerative changes with vacuole formation; here a few red cells are within the limits of the media. Another section shows for a short distance about the middle of the involved area distinct granular degeneration and slight necrosis of the media; this extends through one-third the thickness of this coat, the remainder of which with the adventitia is slightly projected outward.

Sections from Case XVIII show very strikingly a ruptured intima with blood dissecting between that layer and the media. In a vessel of 0.15 mm. lumen in longitudinal section, the intima on both sides for a distance of 0.45 mm. is dissected loose from the media; the layers from the two sides where they are the furthest from the media approach to within 40 microns of each other, thus narrowing the lumen of the vessel to that diameter (Fig. 5). At this point both the intimal layers are almost entirely lacking for a distance of 40 microns, the gap being occupied by red cells, which on the one hand are directly continuous with those in the vessel lumen, and on the other with those beneath the intima. The endothelium is partially absent; the remaining cells are swollen, granular, and contain pigment. In a few places elsewhere than the dissected area, the endothelium and connective tissue of the intima are raised from the elastica for a short distance and leucocytes are in the spaces thus formed.

Nearly opposite the gap in the intima on one side of the vessel the media shows a small area of degeneration that extends almost to the adventitia. This is only a few microns long and the remainder of the media and the adventitia show no bulging. Outside of this for some distance, especially on one side, the adventitia is split into three layers, and in the two spaces thus formed are red blood-cells, the outer collection forming a quite thick mass that extends for some distance in the long axis of the vessel. On the opposite side of the artery the adventitia is also split and has blood

PLATE III.

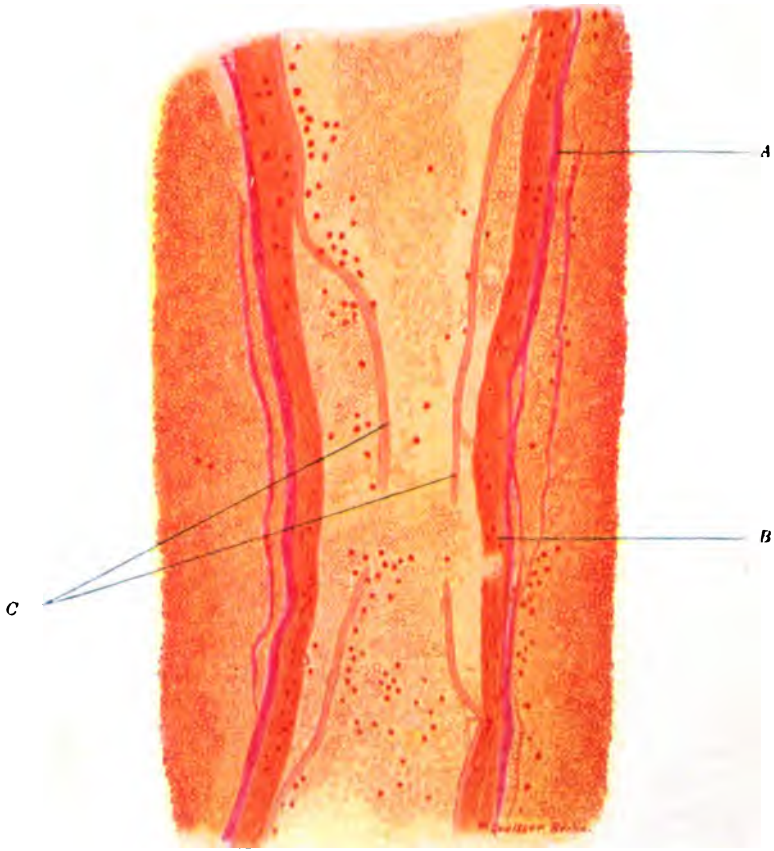


FIG. 5.—CASE XVIII.—Rupture and elevation of intima. *A*, Adventitia showing splitting, blood between the layers. *B*, Media. Just below the pointer is a small area where blood has passed almost through this coat. *C*, Intima which is dissected loose and raised from the media by blood between the two coats. Below the pointers are the places of rupture through which blood has passed beneath the intima. (Leitz, Oc. I. Obj. 5.)

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in the spaces. The whole vessel is entirely surrounded by a mass of blood, the width of which on one side is three times the diameter of the artery itself.

To summarize: the striking changes in the intima of the arteries in this series of brains are two—(1) the lesions of arteriosclerosis or “atherosclerosis” of Marchand. This is so constant in the specimens studied and is so often unaccompanied by, or is more pronounced than, changes in the media that it must be regarded as the primary lesion in these diseased vessels. In addition it may be said that the condition of the elastica as here described points quite clearly to that structure being primarily at fault and lends support to the view taken by Coplin, as based on a study of arteriosclerotic vessels in various tissues other than the brain. (2) Rupture of the damaged intima with consequent dissection of that coat from the media by blood which has passed between the two layers. This lesion is demonstrable in several of the brains in this series and is to the best of my knowledge here described for the first time in connection with the pathology of cerebral hemorrhage. According to Monakow it had not been found previous to 1905, and I have seen no reference to such observation since his statement was made. The significance of this process will be discussed later in connection with the question of aneurysm formation.

b. Changes in the Media.—With the possible exception of one case, the media of the vessels in this series of brains shows no changes that can be regarded as primary, or, in other words, independent of the intimal lesions already described. Lesions of the media are present in many instances in conjunction with the intimal degeneration, but apparently only as secondary or at least accompanying features. These lesions include granular and fatty degeneration, and actual necrosis or disappearance of parts. In some instances blood has extended into this layer through the damaged intima, in a few vessels entirely through the media. The description of such vessels will be taken up later when discussing the pathogenesis of aneurysms. Suffice it to say here that in none of the intracerebral vessels of the brains studied has there been found primary atrophy, colloid or hyaline degeneration, amyloid transformation, or other special change of the media upon which stress has been laid by a number of previous writers upon this subject.

c. Changes in the Adventitia.—These brains contain no vessel from which can be concluded that a change in the adventitia is in any way casually implicated in the degenerative changes of the intima and media already described. The periarteritis pictured by Charcot and Bouchard is conspicuous only by its entire absence. Collections of cells are at times found around aneurysms or ruptured vessels, but otherwise not, even in the numerous instances of extensive intimal changes already described. The changes observed consist in separation of the adventitia from the media by blood, splitting of the adventitia into two or more layers with blood between those layers, and rupture of the adventitia along with the other coats as a part of the phenomena in the formation of false aneurysms. The chief point to be emphasized here is the absence of changes that can be considered primary in this coat of the vessels; periarteritis as a lesion leading to cerebral hemorrhage in this series of cases is therefore absolutely to be excluded.

d. Aneurysms.—In preparations from 16 of the 20 brains of which portions were studied microscopically, there are found in connection with vessels or in cross-section without visible attachment, formations varying from 0.04 to 2.4 millimetres in diameter. These structures are well represented by a specimen from Case I in which such a body of 0.7 mm. diameter is attached to a vessel of 0.05 mm. lumen (Fig. 3). The inner coats of the vessel wall at some distance from the aneurysm show no prominent change except that at one point the intima is thickened and is partially degenerated. Other sections on which the aneurysm is not so centrally placed show such points with a mass of leucocytes and a few red cells beneath and throughout the endothelium and extending through the connective tissue to the elastic lamina. The adventitia is split into two layers on each side of the vessel, the two being separated to some distance by means of blood; this dissection of the adventitia extends to a much greater distance on one side of the vessel than on the other and becomes more marked the nearer the aneurysm is approached. Near the aneurysm, one side of the vessel wall shows pronounced regressive changes. The intima is no longer recognizable, and the media is a granular structure with nuclei only partially visible.

With these changes the vessel continues until at a certain point

the wall, after it abruptly bends outward for a few millimetres on one side, on the other at once almost completely loses its identity and the vessel is represented by the globular structure shown in the figure. The adventitia continues for a very short distance over this mass as a recognizable band, but even here does not stain deeply. The wall of the aneurysm is made up of bands or fibrillæ staining yellowish or brownish-yellow and everywhere separated and infiltrated by red cells and leucocytes. The whole mass is surrounded by a large area of hemorrhage and at some points this is so closely continuous with the content of the aneurysm through the wall that the latter is hardly visible as a boundary, though a distinct rupture is not discernible. The contents of the aneurysm are partly red cells, partly leucocytes; in addition there are numerous areas, rather toward the boundary in location, that stain lightly and are granular in appearance, as though remnants of blood-clot, vessel wall, or other material. No recognizable constituent of the vessel wall is present as a boundary of the entire aneurysm.

Similar formations are found in 15 of the other brains studied, most of them cut at right angles to the vessel so that the latter is not seen. They vary in number in different cases, some showing several in many of the sections from each block, others in sections from one or two blocks only. In a part of those that show attachment to vessels, the adventitia is continued for a short distance from the termination of the vessel proper around the aneurysm, but this is the extent of the demonstrable coats of the vessel. In none of them has elastica been found in the aneurysm wall. In those in which the vessel attachment is shown, as in a section from Case III, the elastica continues only to the margin of the aneurysm and exhibits extensive splitting and fragmentation, as already described under the heading of Changes in the Intima.

The description of other similar aneurysms of various sizes might be almost indefinitely multiplied. It will be noted that in none of them, with the exception of the adventitia extending a short distance in some instances, has any of the coats of the blood-vessel been found to form a boundary; they are therefore, according to the generally accepted classification, spurious or false aneurysms. In addition to those described, the nature of these aneurysms as found in the tissues studied are so well shown by several other specimens that their description is necessary to complete this topic.

In a section from Case XIII is a vessel of 0.03 mm. lumen shown for a considerable distance in longitudinal section. On one side is a saccular aneurysm (Fig. 6), extending outward from the vessel for a distance of 0.165 mm. and parallel to the long axis of the vessel for 0.2 mm. The opening from the lumen of the vessel into the aneurysm, that is, the distance for which the vessel wall is lacking, has a width of 20 microns. The wall of the aneurysm varies from 20 to only one or two microns in thickness. On one side a thin layer of adventitia extends a very short distance over the aneurysm, but with this exception the entire wall stains an indifferent brownish-yellow or slightly reddish-brown (Van Gieson), recognizable structures being absent. It is pigmented throughout. At one point, though not the thinnest, is a secondary bulging of the wall; here the material forming it is irregularly separated into layers and between and largely throughout are red blood-cells. The aneurysm, except for a small area of fibrinous material which also occupies a portion of the outlet from the vessel, is filled by blood which stains fully as well as that within the vessel itself. The entire vessel and aneurysm are surrounded by a large mass of blood which increases in size beyond the latter until it forms a large oval mass that in other sections appears to have bounded a second larger aneurysm. The endothelium of the vessel is present nearly to the border of the opening in the wall on one side; on the other it is not clear for some distance, the cells being swollen or detached and in the thickened part showing numerous quite large spaces which extend to the elastica. The media also shows here slight degenerative changes and pigmentation.

In another section from the same block this aneurysm is shown at another level; at the point of origin the intima of the vessel, inclusive of the elastic layer, is torn and one end is for some distance elevated, that is, extends into the lumen of the vessel as a valve-like flap. Beneath this and extending entirely through an opening in the remainder of the wall, the blood in the vessel lumen is continuous with that in the aneurysm. The degenerated and pigmented media is present on each side of the opening for a little distance before the adventitia is met. In still another section the intima of this vessel, though the latter here bears no aneurysm, shows very extensive degeneration with splitting of the elastica as

PLATE IV.

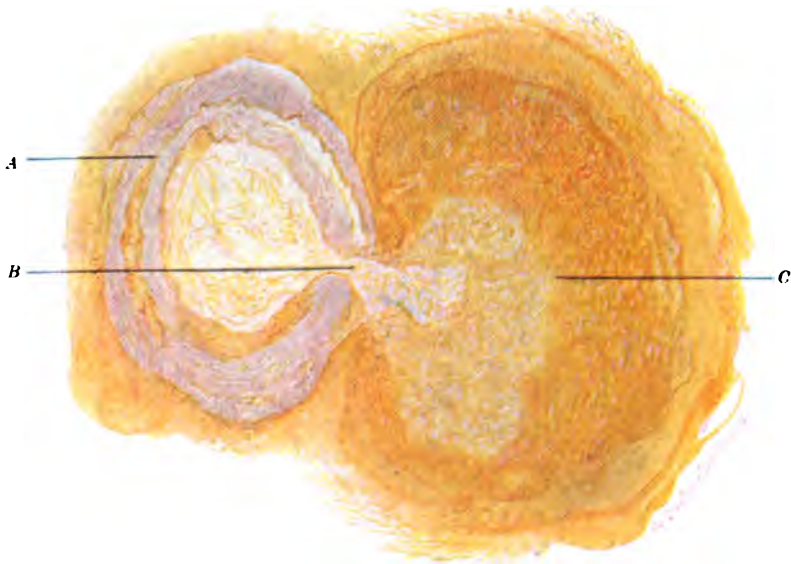


FIG. 7.—CASE XXII.—Vessel and false aneurysm in cross-section. *A*, section of arterio-sclerotic vessel with fibrin and red cells at various points between the layers of the damaged wall; *B*, point of rupture; *C*, false aneurysm largely filled by conglutium resulting from rupture of vessel. (Leitz, Oc. I, Obj. 5.)

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already described when considering the general intimal changes of the series.

Another very definite specimen of false aneurysm is shown on a vessel of 0.2 mm. lumen (Fig. 7), from Case XXII. The aneurysm was approximately 1.5 mm. in diameter in the fresh condition and was situated on a vessel in the internal capsule as a symmetrical globular swelling. The vessel wall here shows marked changes, as will be noted in the further description of this case, consisting of new connective-tissue formation in the intima with partial degeneration, splitting of the elastica, and the presence of blood and fibrin between the elastic layers and between the intima and media. In the section from which the drawing was made there is a clear opening 18 microns wide through both the inner layer of new and degenerated tissue and the outer, the thinned media; the adventitia is not here present or at least is not recognizable. For part of the circumference of the vessel on one side of the opening, the inner zone of new tissue is separated from the outer layer of the elastica, which is closely adherent to the media, by a zone of degenerated tissue that is essentially only an open space. On the other side for some distance the entire structure of the wall is fused into a solid mass. Through the opening in the wall extends a band of fibrin, leucocytes, and red cells which connects the partly fibrinous content of the vessel with that of the attached structure, the latter being a false aneurysm 0.4 mm. in greatest extent. The wall of the aneurysm is formed of lamellated fibrin in the meshes of which are leucocytes and a few red cells. The vessel and aneurysm are surrounded by a larger mass, 1.3 mm. in maximum diameter, of red cells and delicate fibrin net-work, this being bounded by a quite thick compressed band of the same material. This larger mass is clearly the body that was in the gross specimen regarded as an aneurysm.

In Case III, specimens from one block show on the cross-section of a vessel of 0.05 mm. lumen a false aneurysm a trifle greater in diameter than is the vessel itself. On one side the adventitia possibly extends for a very short distance over the aneurysm, but its identity is questionable. The remainder of the wall, which is quite thick, is composed entirely of the rather dense, yellowish-staining fibrinous or indefinite material that bounds these aneurysms in

general. The opening connecting the vessel lumen with that of the aneurysm is entirely clear for a width of 5 microns; bordering it are red cells attached to the degenerated vessel wall. In both vessel and aneurysm are red cells and many leucocytes. The intima and media of the vessel are fused into an almost homogeneous layer; at one point near the aneurysm the adventitia is split and separated to form a wide, oval space containing partly degenerated red cells and leucocytes.

The presence of large numbers of false aneurysms in the sections of tissue studied led to the question as to whether they were structures similar to those isolated in the gross specimens. The latter were regarded as without doubt the miliary aneurysms so much discussed since the publication of Charcot and Bouchard. Were these true aneurysms or were they the false type such as were found in the sections? The most reasonable supposition was that they were of the same nature as those found in the sections, since the blocks from which the latter were cut were of tissue continuous with the lacerated parts in which the gross aneurysms had been found. In order definitely to decide this point, I serially sectioned freshly isolated and immediately hardened aneurysms from Cases III, XI, XII, XIII, XXII, XXIV, and XXVI. Some of these represented clusters of aneurysms, three to five in number, others were single globular or fusiform masses with the vessel bearing them visible for some distance at one or both poles. The findings, some of which have already been mentioned under preceding topics, were the most instructive in this study. *Not one of these structures proved to be a true aneurysm.* They were simply masses of blood, fluid or partly coagulated, enclosed by walls of indifferently staining material, possibly in some instances degenerated remains of the vessel wall, in many cases demonstrably fibrin.

One of these aneurysms with the vessel projecting from opposite poles was from Case XXII. It was nearly two millimetres in diameter. The vessel on one side at some distance from the aneurysm was purposely doubled in embedding so that a number of longitudinal sections were obtained in addition to the transverse ones through the remainder of the vessel and the aneurysm. Microscopically the vessel on one side of the aneurysm shows proliferative changes in the intima with new connective-tissue formation and

also degenerative changes much more marked at some points than at others. At certain places the degeneration is specially pronounced in the peripheral part, forming a distinct space between the inner portion and the outer layer of the split elastica. The latter is split into many layers, some of the finer of which are among the new connective tissue. Between the layers are scattered red blood-cells. A small mass of fibrin and red cells surrounds the vessel at a short distance from the aneurysm. The media is here intact. As the aneurysm is approached the changes in the intima become more pronounced. At one place for nearly one-fourth the circumference the elastica has entirely disappeared and the media shows granular degeneration and fragmentation. Further on the media is markedly thinned and at points shows bulging. In the spaces between the outer portions of the degenerated intima, and extending at one point into and almost or quite through the latter, is a mass of fibrin containing in its meshes a few red blood-cells. Finally there appears a direct opening through the entire wall with the formation of a false aneurysm as already described in connection with Fig. 7, which was made from this specimen.

The further changes in the vessel consist in a gradually increasing degeneration of the coats, which collectively stain less intensely and merge with the wall of the aneurysm as a mass of indifferently staining material among, or by the side of, threads of fibrin. Finally there is left only a small space to mark the site of the vessel, the aneurysm wall having also disappeared. Around this space are numerous phagocytic or "contractile" cells. In the sections showing progressively these changes, the mass of blood and fibrin surrounding both the vessel and the aneurysm increases in size; when the vessel and aneurysm have finally disappeared there is left only this mass, with its denser boundary, to represent the aneurysm (?) which was observed macroscopically. No distinct point of rupture in the false aneurysm has been found, though in many places the wall is infiltrated by leucocytes and red cells. As the opposite extremity of the mass of blood is approached, degenerated fragments of the vessel wall are again met. In an order the reverse of that described, the wall becomes more perfect until the vessel is again present, still showing, however, the intimal degeneration as before described; it is also surrounded by a narrow and

decreasing sheath of fibrin and blood as observed at the opposite pole of the aneurysm.

This specimen, then, shows very clearly extensive intimal disease of an artery, with blood in and between the layers of the intima, then between it and the media, and finally extending through the latter, thus forming a false aneurysm when the adventitia disappeared, as shown in the figure. The body that had in the gross specimen appeared as a typical globular miliary aneurysm was therefore only the collection of blood and fibrin resulting from the rupture of the vessel, and bounded only by fibrin containing small fragments of brain tissue. A part of the phenomena of the rupture of the vessel was the formation of a false aneurysm.

Another very instructive specimen in the way of showing the nature of a supposedly miliary aneurysm was found in Case XXVIII. The specimen was a globular enlargement of a vessel with a slight continuation from one pole, though not extensive enough to make it a typical fusiform aneurysm. Sections cut as in the preceding specimen show a vessel of 0.15 mm. lumen with pronounced intimal changes as before described. There is blood between the intimal layers and also at a few points extending through that structure, where it is most damaged, until the cells are in contact with the media; the latter, however, is not a prominent feature. The media also at points shows moderate regressive changes. The adventitia is not everywhere visible, but this is apparently due to a mechanical rather than degenerative cause. The vessel can be traced through every section mounted and nowhere shows aneurysmal dilatation; rupture is not observed, though from the appearance of the wall extravasation might readily have occurred. As in the other instances, the globular mass simulating an aneurysm is a collection of blood surrounding the vessel and bordered by a very thin rim of fibrin, with, in many sections, a band of brain tissue enclosing the latter.

The source of hemorrhage here is curiously enough a false aneurysm on a smaller vessel, possibly a branch of the larger though not so shown, at some distance from the latter and nearer the centre of the blood mass. This small vessel shows degenerative changes such as have been described in other cases and finally is transformed into an aneurysm. That this gave rise to all the hemorrhage cannot

be positively stated, though from the larger vessel certainly not more than slight extravasation had occurred. However this may be, here was what appeared to be a typical macroscopic aneurysm, attached to a vessel which microscopically is shown to be absolutely without dilatation or even detectable rupture.

In Case XXIV, in addition to partial destruction of the caudate nucleus and thalamus of the right side, there was a small hemorrhagic focus 1.5 centimetres in maximum length near the central part of the pons. In this space was a small blood-vessel with one end free and bearing laterally a slightly oval aneurysm 3 mm. in extreme length, this corresponding to the long axis of the artery. In the outer portion of the sac was an opening nearly half its length, clearly the point of rupture. After a drawing had been made of the specimen (see Fig. 8), which resembled very much that pictured by Gull, it was embedded and sectioned serially with results essentially as in the others described. The vessel shows pronounced changes in the intima, consisting at various points of enormous swelling with granular and vacuolar changes in the endothelium, formation of cellular tissue on the surface of the intima, duplication of the elastica, and regressive changes. The media is mainly intact. The vessel was sectioned in the longitudinal direction and a clear point of rupture was not found, though the vessel ends abruptly at a damaged area corresponding to the situation of the aneurysm and is similar here to those places in other vessels showing rupture. The supposed aneurysm, as in the other instances, is only a collection of blood in the cerebral tissue with enough fibrin to increase slightly the consistency and resistance. Nowhere is there aneurysmal widening of the vessel. The specimen then is only a false aneurysm, the fragile boundary of which had given way at one point and thus produced the larger hemorrhage.

In addition to the case just described, macroscopically ruptured aneurysms were found in three other brains, Cases IV, XI, and XII, making four in all in which this feature was observed. In three of the cases the sac was not sectioned. As Case XXIV included the vessel bearing the sac, it has been described in that group. In one of the aneurysms in Case XII the sac, still attached to the vessel and showing a small rupture, has been preserved as a gross specimen (Fig. 2). Another from the same case was sectioned.

These gross specimens appeared as segments of quite thin sacs partly embedded in the wall of the hemorrhagic areas, and empty or containing a small quantity of adherent blood; the other parts of the sacs had evidently been entirely fragmented or else carried away in the *débris* and coagulum. In one the sac, broken at about the midpoint, was 0.6 cm. across. Microscopically these sacs show exactly the same changes as do the smaller ones, namely, a boundary of fibrin and compressed or slightly involved brain tissue to which masses of partly clotted blood are adherent. Absolutely no recognizable structural elements are present. At one point in the wall of the largest is another aneurysm 0.1 mm. in diameter, more than one-half of which projects into the larger; the latter by its encroachment upon the cerebral tissue as it enlarged had partly surrounded and enclosed the smaller, thus furnishing unmistakable proof that the larger was not a true aneurysm.

These findings from (1) scores of aneurysms in sections of tissue, (2) the serial sectioning of aneurysms with the vessel at each pole, and (3) the microscopic study of macroscopic ruptured aneurysmal sacs, constitute in my opinion a complete demonstration of the character of these so-called miliary aneurysms. They are false aneurysms bounded by fibrin and involved portions of brain tissue or by fully degenerated and hence unrecognizable elements of the vessel walls.

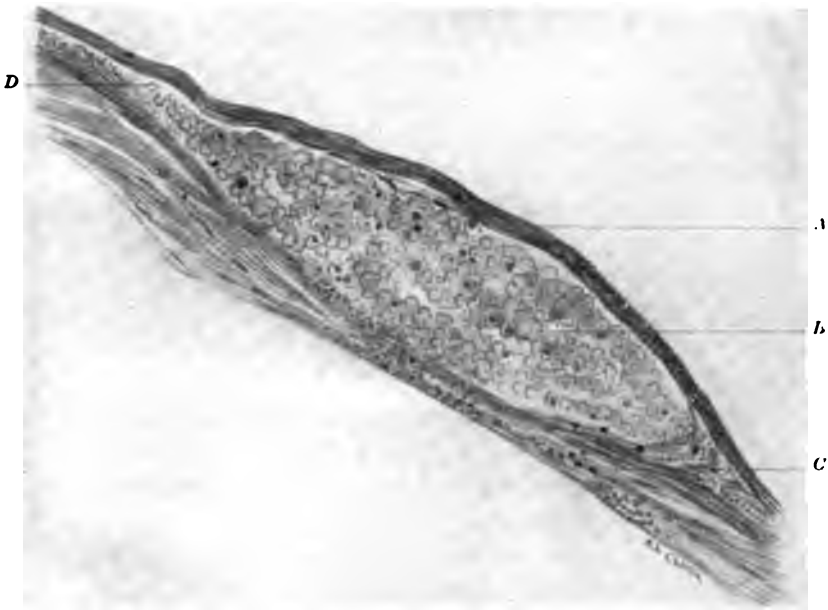
e. Method of Formation of False Aneurysms.—The vascular lesions in these brains have been described with sufficient detail to show that the intima is the coat primarily and most extensively diseased. That this intimal lesion is responsible for the further changes, including the production of aneurysms, is not to be doubted; but the exact method of aneurysm formation is not so clear. The very nature of the aneurysms described makes it difficult to distinguish in all instances between aneurysm formation by the gradual yielding at one point of a wall first weakened by a diseased intima, and the same result produced by blood which at first worked its way between the layers of the wall—the so-called dissecting aneurysm. A majority of the writers upon this subject regard the dissecting aneurysms as bearing no relation to the miliary type. Eichler has already been quoted as saying that dissecting aneurysms are to be sharply separated from the miliary.

FIG. 8.



CASE XXIV.—Vessel in pons bearing a false aneurysm in which is a linear rupture. Two diameters.

FIG. 9.



CASE XV.—Dissecting aneurysm. *A*, adventitia; *B*, media; *C*, collection of blood between media and adventitia. Further dissection between these layers is in progress at *D* (*B & L*, Oc. I, Obj. 2.)

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The former, he says, are simple hæmatomata of the vessel wall; they are never the cause, but are the result, of hemorrhage. Monakow states that aneurysma dissecans is a formation *sui generis* which has nothing to do with miliary aneurysms.

These statements are evidently based on the supposition that the miliary aneurysms are true aneurysms in the sense of being dilatations of vessels still bounded by one or more coats of the vessel, without any two of them having previously been separated by blood, in other words, lack of dissection. According to the usual classification the miliary aneurysms in my specimens must be denominated false aneurysms. This separates them from the dissecting form which has for its boundary one or more coats of the vessel; according to most writers the boundary is the adventitia, since they speak of dissecting aneurysms as collections of blood in the space between that coat and the media. This difference between the dissecting aneurysm and the fully formed miliary aneurysm as I have found the latter may therefore be conceded; that they are in every case distinct in the sense of not being stages in the same process, I am not ready to believe. On the contrary, the findings in some of my cases indicate very clearly that the false aneurysms there present, and which in the gross specimens appeared as the miliary type, began as the dissecting variety.

Dissection of blood between the intima and media without further prominent change in the vessel wall has already been described in two cases under the head of Changes in the Intima, one of them being shown in Fig. 5. Of great significance in this connection is the aneurysm described under Fig. 6, although the point to which reference is now made, as there stated, is brought out by a section at a different level and hence not shown in that drawing. The fact that the vessel itself exhibits absolutely no dilatation, the intima continuing in a straight line except where a flap starting from the degenerated and ruptured point is raised to form an opening through which the blood has passed, shows very definitely that this aneurysm began as the dissecting type. As the aneurysm itself is a typical false aneurysm, the relation of the dissecting form to the latter is thus well shown, although of course the stage with a collection of blood immediately beneath the adventitia cannot be demonstrated because that structure as such has disappeared.

That blood dissects through the media is shown by several of my cases. In Case XV is an artery of 0.8 mm. lumen, the intima of which is a thickened, indifferently staining, pigmented layer possessing no elastica. The media stains by Van Gieson a rather homogeneous yellowish-brown, though in some parts the muscle fibres can easily be distinguished. At one point in the wall the thickened intima is separated into irregular layers and between them is blood. Columns of red cells at points extend also into the media, in one instance occupying a space 46 microns long where the media has practically disappeared, leaving only an exceedingly thin film of that layer between the blood and the adventitia. At another place in this wall (Fig. 9), is an oval collection of blood 0.15 mm. in length between the media and adventitia. The latter coat is very slightly elevated; but the space for the blood is obtained largely at the expense of the media, which is greatly compressed under this area and with the intima is displaced inward, encroaching sufficiently upon the lumen to slightly more than overcome the concavity of the vessel wall.

Passage of blood through the intima and media is further shown in a vessel of 0.15 mm. lumen in Case VII. At one point there is a diagonal opening with a maximum width of 11 microns extending entirely through intima and media, this channel being densely packed with red cells that are in direct continuity with those in the lumen of the vessel. At this place in the wall, and for some distance on the side toward which the diagonal opening points, the adventitia is split into layers which are elevated to various distances, the spaces under and between them being occupied by blood. At various points these adventitial layers cannot be clearly traced through the entire mass of blood, which is thus apparently continuous with that outside the vessel. Bordering the opening through the wall, the intima and media show pronounced degenerative changes. There is a fairly large hemorrhage surrounding the vessel, which in other sections exhibits extensively damaged intima and media but no rupture. This vessel is an example then of rupture of the two inner coats with splitting and wide distention of the adventitia and at least extravasation of blood through the latter coat into the surrounding tissue.

That a part, possibly the greater part, of the false aneurysms

found in these cases began therefore as the dissecting type appears to be fully established by these specimens. That some of the aneurysms arose from simple yielding of a diseased wall without dissection of the coats has also been clearly shown by preparations described under other headings. Hence the conclusion must be that the false or so-called miliary aneurysms may be produced by either of these two methods. To the dissecting aneurysm therefore must be attributed a much greater significance than it has hitherto received.

f. The Actual Source of Hemorrhage.—Monakow states that miliary aneurysms have been recognized by all later observers as an essential cause of bleeding, and are regarded to-day as the most certainly established source of cerebral hemorrhage. The disputed question now, he says, is whether they are the only cause; can vessel changes of other types, as atheroma, hyaline degeneration, etc., lead to bursting of vessel walls? This question as propounded by Monakow presupposes that the miliary aneurysms are special structures and that one or more coats of the vessel still persist. In the light of my findings this question must be put in a different way, namely: is the bursting of these relatively slowly formed false aneurysms, or the blowing out, so to speak, of a segment of diseased but not aneurysmal vessel wall, without subsequent aneurysm formation, the source of hemorrhage? Or may both be responsible?

The findings in this series of brains indicate that both these methods are active in producing cerebral hemorrhage, the false aneurysms probably in the majority of instances. The presence in the gross specimen, in four of these cases, of ruptured aneurysmal sacs, with later microscopic study of three proving them to be false aneurysms, shows clearly that those structures rupture. In one, that of the small hemorrhage in the pons, the entire bleeding can unquestionably be attributed to this source. In some of the larger hemorrhagic areas, with their widespread destruction of tissues, the aneurysm there found may possibly have been torn by the disruption which followed hemorrhage elsewhere, though this can hardly be regarded as the most reasonable supposition.

In the sections of tissue a clearly defined rupture of the wall of one of these aneurysms has not been found, but in many of them the condition of the wall and of the surrounding tissues justifies

the belief that they were the source of hemorrhage. In others, with thick fibrinous boundaries and the lumen itself largely filled by coagulum, it is very probable that hemorrhage would more readily occur from other parts of the diseased vessel wall than from the aneurysm itself. This in fact is shown in the case of one vessel, an unruptured false aneurysm which has already been described. This vessel in another section, some distance from the aneurysm, shows almost entire disappearance of the intima and for a long distance the media is degenerated. For one-third the circumference the adventitia is split and blood is between the layers. At a point on the opposite side of the vessel all three coats are lacking and through an opening 40 microns wide the content of the vessel is in direct continuity with the blood mass outside of and surrounding it. Here then is a clear instance of rupture of a diseased vessel without aneurysm formation. Furthermore, the same vessel bears at another point a false aneurysm, of the same diameter as the artery, which is unruptured; this is evidence that a diseased vessel wall can be less resistant to the pressure of the blood stream than is an aneurysm containing a coagulum. That intracerebral vessels rupture without previous aneurysm formation is another point that this study, so far as I am aware, demonstrates for the first time, in stained sections of tissue, in this connection.

That the large hemorrhages, with their terrific destruction of tissue, so often found in cases of apoplexy, are as apt to occur from primary rupture of vessels as from the bursting of false aneurysms, I do not believe. Laying aside, however, the question of massive hemorrhages, the fact that rupture of small arteriosclerotic intracerebral arteries takes place is of great interest in connection with the pathogenesis of small hemorrhages that give rise to paralyses and other non-fatal affections.

As this study was undertaken for the purpose of determining the pathological changes in the intracerebral vessels in cases of spontaneous cerebral hemorrhage, that aim has been strictly followed. Certain subsidiary points are usually considered in this connection, however, and these were noted in addition to the principal theme of the study. These points deal with the condition of the arteries at the base of the brain, the left heart, and the kidneys, and my findings are here briefly set forth as a supplement to what has already been described.

CONDITION OF THE BASAL VESSELS

The relation between lesions of the great vessels at the base of the brain and of the intracerebral arteries has given rise to much discussion. Löwenfeld states that an etiologic relation of atheroma of the basal arteries to cerebral hemorrhage can be assumed in only a part of the cases. It appears that changes in the basal and in the intracerebral arteries develop usually, possibly always, independently of each other. Only in advanced endarteritis of the former, he believes, can the latter be directly affected, namely, by increase of blood-pressure.

The condition of the basal vessels was noted by Charcot in 69 cases as, very atheromatous, 17; moderately atheromatous, 12; slightly atheromatous, 25; unchanged, 15. He says there may be marked atheroma of the basal vessels and the branches to the meninges without the presence of miliary aneurysms in the brain, or there may be numerous miliary aneurysms with practically no lesion of the basal vessels; they may, however, and frequently do, coincide.

Weiss found in 13 cases of fatal hemorrhage, 9 brains with extensive, 4 with moderate arteriosclerosis of the basal vessels. Eulenberg found in his 42 cases, 29 with disease of the basal vessels.

As the intracerebral vessels in my series show simply arteriosclerosis instead of a special pathologic process peculiar to cerebral apoplexy, one might regard as probable a relation between its presence or severity in them and in the arteries of the base. In a general way, although there are exceptions, my cases support this postulate. In only two of the brains, Cases XVII and XXI, was atheroma of the basal vessels entirely lacking. The first was from a man of 46 years, the corpus striatum of the right side being the site of hemorrhage. The laceration of cerebral tissue was very slight as compared with most other specimens studied, there being little more damage than a cleft through the ganglion; this was bordered by, for these cases, unusually firm and smooth brain substance in which only a few small hemorrhagic foci were visible. No macroscopic aneurysms were found in the fresh specimen or in the portions that were macerated. Microscopically the intracerebral vessels show no noteworthy lesions. In the border of the large area was found nothing to explain the occurrence of hemorrhage.

The second brain without basal atheroma was from a woman of 53 years. In it was no visible laceration and hence no evident source of the blood, which was present in all the ventricles. No aneurysms were present. In the macerated specimen were no aneurysms or other lesions except in one artery 0.2 mm. in diameter, which showed several tiny areas slightly yellow in color. This brain was not studied microscopically.

Of the four brains in which the basal vessels showed but slight atheroma, that is, a few small, widely separated patches, macroscopic aneurysms were found in but one. Two of the brains were thoroughly studied microscopically and showed small aneurysms in the sections, but the arteriosclerosis was in general less marked than in most of the specimens with more extensive basal lesions. One of the three aneurysms found in the third brain of this list was sectioned, the artery bearing it showing pronounced arteriosclerosis.

In seven brains with moderate atheroma of the basal vessels, that is, numerous patches but none of great length and with moderate rigidity, and nine with advanced atheroma, that is, numerous confluent patches or long uniform areas and marked rigidity, no noteworthy differences in the microscopic lesions of the intracerebral vessels are present. One of the former list shows considerably less involvement than the others, but in general the two groups could in no wise be separated by the microscopic findings. Four in each of the groups were not studied microscopically.

The findings as regards macroscopic aneurysms when compared with the condition of the basal vessels are of interest. Macroscopic aneurysms were found in the cerebral tissues in 11 of the 14 cases of advanced basal atheroma, in 8 of the 11 cases of moderate atheroma, in 1 of the 4 cases of slight atheroma, and in neither of the 2 cases with no atheroma. Tabulated, the findings in the four degrees of atheroma are:

Advanced,	14 cases.	Macroscopic aneurysms in 11 or 79 per cent.
Moderate,	11 cases.	Macroscopic aneurysms in 8 or 73 per cent.
Slight,	4 cases.	Macroscopic aneurysms in 1 or 25 per cent.
None,	2 cases.	Macroscopic aneurysms in 0 or 0 per cent.

Thus so far as the presence of aneurysms is concerned, there was a constant rise in the percentage of positive cases as the basal atheroma increased in severity. The moderate and advanced groups

differed the least, as they also do in the microscopic lesions. Aneurysms were absent, however, in cases, three of each, of both moderate and advanced atheroma of the basal vessels, thus supporting the statement of Charcot that they may not accompany such lesion. They were also found in one of the four cases of slight sclerosis.

Concerning the brains in this series of thirty-one cases therefore, we can in general say that in both its macroscopic and microscopic manifestations, arteriosclerosis of the intracerebral vessels was the more pronounced as atheroma of the basal vessels increased in severity. A point that should be investigated in this connection is the condition of the intracerebral arteries in brains showing various stages of basal atheroma but in which hemorrhage has not occurred. The time at my disposal unfortunately did not permit the study of this phase of the subject.

CONDITION OF THE HEART

A second lesion of importance in connection with cases of cerebral hemorrhage is hypertrophy of the left ventricle of the heart. This affection is so intimately associated with those of nephritis and general arteriosclerosis that a discussion of any one of the three initiates what may with propriety be called a vicious circle in argumentative medicine. For this reason it will answer my purpose to consider briefly the opinions of some other writers and then give my own findings.

Eulenberg states that hypertrophy of the left ventricle can favor hemorrhage only when it permanently raises the normal mean tension of the aortic system. He found hypertrophy of the left ventricle in 6 of the 29 cases in which the basal vessels were diseased, and in 3 of the 13 cases in which they were normal, a total of only 9, or 21 per cent., in 42 cases.

Charcot found hypertrophy of the heart in 22 of 55 cases in which this point was noted, but in only 36 per cent. was this a simple hypertrophy, the only type that can be accused of increasing arterial tension. Weiss reports pure hypertrophy of the heart in 12, or 40 per cent., of his 30 cases of hemorrhage.

Kaufmann states that as an essential influence in causing rupture of diseased vessels the chief factor is hypertrophy of the heart

without dilatation, especially of the left ventricle, of the type that is found in contracted kidney. Monakow ventures no positive opinion upon the subject.

The condition of the heart was noted in 30 of my cases, 17 women and 13 men. Of the former, 8 showed hypertrophy of the left ventricle, 5 of both ventricles, and in 4 the heart was normal. Of the 13 men, the left ventricle alone was hypertrophied in 12, both ventricles in one. Regarding the nature of this hypertrophy, I can say that in only 6 cases, all women, was there demonstrable valvular lesion. In each the mitral valve was affected. The lesions in the 4 with hypertrophy of the ventricle alone were "chronic mitral endocarditis" in two, "mitral stenosis and insufficiency" in one, and "verrucose endocarditis of mitral and tricuspid" in one. In the remaining two of the 6 cases, with both ventricles hypertrophied, the lesion was classified as "mitral insufficiency." The percentage of cardiac hypertrophy uncomplicated by valvular lesion is therefore 41 per cent. in the women of this series, this corresponding quite closely to the figures quoted. In the male subjects the percentage of hypertrophy of the left ventricle, without valve lesion, is 100, an unusual finding.

Whether the hypertrophied heart plays a rôle in causing the arteriosclerosis leading to cerebral hemorrhage, or in the opposite manner its hypertrophy be induced by changes in the arterial system of which that of the brain forms a part, the actual effect of simple hypertrophy of the left ventricle upon diseased cerebral vessels can be only one, namely, to hasten their rupture. With the intracerebral vessels, from whatever cause, showing the lesions described in this paper, a rising blood-pressure due to increasing hypertrophy of the heart is of vital importance in precipitating fatal hemorrhage. More than this we are probably not in a position to say.

CONDITION OF THE KIDNEYS

As was mentioned when considering the heart, nephritis is one of a triad of conditions which is impossible to weigh separately. If in a certain case contracted kidneys be the cause of cardiac hypertrophy, then, through the action of the latter upon the cerebral vessels, the nephritis may possibly play the initiative rôle in the production of cerebral hemorrhage. Löwenfeld states that con-

tracted kidney must be given a place among the causes of this lesion, while Monakow regards it as certain that cerebral hemorrhage in nephritic subjects is due to no uniform cause.

I cannot see that my series of cases aids in clearing the obscurity surrounding this question. The 30 cases in which the condition of the kidney was noted are thus grouped: interstitial nephritis, 10; parenchymatous nephritis, 12; diffuse ("parenchymatous and interstitial"), 6; arteriosclerotic contracted kidneys, 1; normal, 1. These were diagnoses from the gross specimens, routine microscopic studies not being made. From this will be seen that though in only one case the kidneys were normal, the remainder showed no uniform lesion. Not only were the groups interstitial, parenchymatous, and diffuse demonstrable, but the individual cases showed various degrees of involvement ranging from slight acute parenchymatous nephritis to the typical contracted kidney. To relatively few of the interstitial group could be ascribed a primary part in the arteriosclerosis and cardiac hypertrophy, even if in general one were inclined to favor such view.

CONCLUSIONS

1. The lesion of the intracerebral arteries in cases of spontaneous cerebral hemorrhage is primary in the intima, beginning apparently in the elastic layer, and is simply arteriosclerosis, or atherosclerosis, differing in no wise from that process as it is found elsewhere in the body.

2. In some cases this lesion progressively involves the media and adventitia and leads at points to such weakening that simple rupture of the vessel wall takes place.

3. A circumscribed portion of the intima of an artery may give way and permit blood to pass between the coats of the vessel, forming the so-called dissecting aneurysm.

4. Both the simple rupture of the vessel wall and the dissecting aneurysm are followed by the formation of false aneurysms, though such formation does not occur in every instance.

5. The so-called miliary aneurysms of cerebral hemorrhage are false aneurysms, due primarily to arteriosclerosis, and are preceded by simple rupture or by dissecting aneurysm, probably more often the latter, of the affected artery.

6. Spontaneous cerebral hemorrhage occurs both from the rupture of false aneurysms and the rupture of vessels without previous aneurysm formation.

7. In general, but not invariably, the intracerebral arteriosclerosis corresponds in severity to that of the arteries at the base of the brain.

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